The Peter T Bohan
Memorial Lectures on Medicine

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TO

THE STUDENTS OF DR PETER T BOHAN

WHEREVER THEY MAY BE

FOREWORD

The Peter T Bohan Memorial Lectureship has been made possible in perpetuity by Doctor Bohan s former students by physicians who, although not his students in their undergraduate days yet came under his instruction when they attended his clinics and by persons not professionally concerned with medicine who nevertheless wish to share in honoring a great clinician and great teacher

The seven lectures here published happily were delivered while Doctor Bohan lived More of them would have been given in his lifetime had he not delayed inception of the series by his insistence that he did not deserve such recognition as the establishment of a lectureship bearing his name

Yet Doctor Bohan exemplified in high degree those qualities that among practitioners and teachers of medicine are accepted as deserving of honor He could perceive and impart Analyzing selecting discarding he overcame the various factors that confuse diagnosis and then presented in understandable fashion the salient features in the case under consideration As a result each clinic implanted in the student s mind a sound thought on which he could draw ever after as from a never failing spring

C F Dixon M D

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Pernicious Anemia from Addison to Folic Acid

Russell L. Haden M D
1947

A constantly fatal disease unexplained at autopsy is always intriguing The mysterious nature of pernicious anemia thus interested Thomas Addison[1] when he described the first group of patients in 1849 He said this is a remarkable form of anemia which has not attracted the attention it really deserves The anemia was profound and of unknown origin The patient became progressively weaker with little wasting and finally died without response to any treatment. A post morten examination did not aid in explaining the problem No real progress was made in solving the puzzle until the discovery of the beneficial effect of liver feeding in 1926 by Minot and Murphy[2] completely altered the outlook of the patient Further research is slowly unraveling the mystery Clinicians still think however, of pernicious anemia as a remarkable form of anemia

It is my purpose to discuss historical highlights of this interesting disease from the time of Addison to the discovery of folic acid and to emphasize some important clinical aspects

Idiopathic pernicious anemia is a disease of nutrition characterized by macrocytic anemia histamine refractory achlorhydria combined sclerosis of the spinal cord and a specific response to liver and liver substitutes The anemia alone may be completely relieved by a single chemical compound pteroylglutamic acid (folic acid) The clinical picture is variable the anemia may be minimal only about three



Russell Landram Haden

Russell Landram Haden was born in 1888 in Palmyra Virginia He graduated from the University of Virginia in 1910 and obtained his M D degree from Johns Hopkins University in 1915 After a period of residence in Johns Hopkins and Henry Ford hospitals—at the latter he served as director of laboratories—Dr Haden joined the faculty of the School of Medicine at the University of Kansas where from 1923 to 1930 he was Professor of Experimental Medicine In 1930 he became head of the department of medicine at the Cleveland Ohio Clinic In 1929 he was awarded a gold medal by the Radiological Society of America for his contributions to dental roentgenology He is the author of *Clinical Laboratory Methods* 1923 *Dental Infection and Systemic Disease* 1928 *Principles of Hematology* 1939 He died in 1952

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fourths of the patients have signs of a cord lesion initially a loss of vibratory sense is usually the earliest and often the only evidence of neurologic involvement achlorhydria is a constant finding

It is a disease of older people In 427 patients studied at the Cleveland Clinic only 5 were less than 30 years of age In a total number of 579 I have seen, the anemia began in only one individual less than 20 years of age Fifty two per cent of the patients were between 40 and 60 A very large proportion were over 60 when the diagnosis was made

Numerous clinicians, beginning with Combe in 1822[3] reported fatal unexplained cases of anemia which we now recognize as pernicious anemia Thomas Addison however, first in 1849 and again in 1855 described it as a clinical entity

Why was the disease so called? Addison in his original description speaks of it as a remarkable form of anemia Its approach is first indicated by a certain amount of languor and restlessness to which presently succeeds a manifest paleness of the countenance The symptoms go on increasing the patient experiences a distressing and increasing sense of helplessness and faintness he dies either from sheer exhaustion or death is preceded by signs of passive effusion or cerebral oppression [4] All patients in this group were not suffering from true pernicious anemia since two recovered and in three disease of the adrenal was found at autopsy Addison said in 1855 that he was trying to throw additional light on

this condition when he discovered the disease of the adrenal glands known as Addison s disease He again emphasized that there was no discoverable cause whatever

Addison recognized the anemia only by the pallor of the skin and the thinness of the blood In 1849 no blood cell counts or hemoglobin estimations had been done Vierordt[5] did the first red cell count in 1851 Funke[6] discovered hemoglobin the same year, and Welcher[7] published the first extensive clinical article reporting blood counts and hemoglobin estimations in numerous diseases in 1854 Thus accurate measurements of the blood came after Addison s original communication

Addison s observations made little impression even in England, and little more was heard of this remarkable anemia until it was reported independently by Biermer[8] in Switzerland in 1871 At a meeting of the Medical Society in Zurich, November 6 1871 Biermer under the title of Progressive Pernicious Anemia described 15 cases of severe anemia He used the name only in a symptomatic sense grouping together anemias of widely different etiology He had previously[9] mentioned similar cases in which he emphasized fatty degeneration of the heart and vessels Biermer stressed the role of pregnancy So some cases he described were evidently what we know now as the anemia of pregnancy His group has been described as a provisional shelter for a multitude of cases [10] He did not think of pernicious anemia as a

sıngle dısease He agaın emphasızed the fındıng at autopsy of fatty degeneratıon of the heart muscle and small vessels

Bıermer s report was publıshed ın 1872 ın the proceedıngs of the Medıcal Socıety ın Zurıch For some unknown reason ıt quıckly excıted the ınterest of clınıcıans everywhere Artıcles on progressıve per nıcıous anemıa began to appear rapıdly In England, Addıson s orıgınal descrıptıon was not recalled untıl stımulated by Bıermer s work In 1875 Wıllıam Pep per[11] ın Phıladelphıa wrote an extensıve artıcle of twenty sıx pages on the dısease ın the *Amerıcan Jour nal of Medıcal Scıences* Pepper says, My present purpose ıs to offer a contrıbutıon to thıs ımportant study by callıng attentıon to a pecular form of ane mıa of obscure and fatal character whıch has recently been redescrıbed (ı e by Bıermer) as though ıt were a new affectıon under the name of Progressıve Pernı cıous Anemıa He then emphasızes that Addıson had prevıously descrıbed the dısease as ıdıopathıc anemıa Pepper s maın contrıbutıon ıs hıs dıscovery of the extreme hyperplasıa of the marrow He con sıdered pernıcıous anemıa as a prımary dısease of the bone marrow

Many papers on the subject were publıshed be tween 1875 and 1878 In 1878 Eıchhorst s extensıve monograph [12] of 375 pages entıtled Progressıve Per nıcıous Anemıa appeared All cases prevıously re ported were revıewed Eıchhorst mentıoned Addı son s work but gave hım lıtle credıt Addıson he

said considered the anemia due to fatty degeneration of the internal organs while we now know that the anemia is primary and the fatty degeneration is secondary Eichhorst described as pernicious anemia cases of anemia which we now exclude The term designated only a group of fatal anemias and included such conditions as true aplastic anemia leukemia and other bone marrow diseases as well as severe anemias due to infection and toxemia Eichhorst did not have our present concept of pernicious anemia as a single specific entity The name he used however, has persisted Interest stimulated by these early papers has never abated

Pernicious anemia is defined as a macrocytic anemia—the red cells are characteristically large Eichhorst mentions macrocytosis but reports no measurements or even counts in his own cases He does say the number of red cells was about one tenth or one twenty fifth of normal The first blood count in a patient with pernicious anemia seems to have been done by Sørensen[13] in 1874 when he counted the blood with Malassez s apparatus and found only 470 000 red cells Sørensen also emphasized the large size of the cells The diameter of red cells had been measured from the time of Leeuwenhoek [14] A monograph on the dimensions of red corpuscles by Manassein[15] had appeared in 1872 Eichhorst concluded that the diameter of the cells is almost always increased [16] Laache in his book on the anemias[17] published in 1883 has a *long discussion* of pernicious ane

single disease He again emphasized the finding at autopsy of fatty degeneration of the heart muscle and small vessels

Biermer s report was published in 1872 in the proceedings of the Medical Society in Zurich For some unknown reason it quickly excited the interest of clinicians everywhere Articles on progressive pernicious anemia began to appear rapidly In England, Addison s original description was not recalled until stimulated by Biermer s work In 1875, William Pepper[11] in Philadelphia wrote an extensive article of twenty six pages on the disease in the *American Journal of Medical Sciences* Pepper says My present purpose is to offer a contribution to this important study by calling attention to a peculiar form of anemia of obscure and fatal character which has recently been redescribed (i e by Biermer) as though it were a new affection under the name of Progressive Pernicious Anemia He then emphasizes that Addison had previously described the disease as idiopathic anemia Pepper s main contribution is his discovery of the extreme hyperplasia of the marrow He considered pernicious anemia as a primary disease of the bone marrow

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anemia should never be diagnosed if free hydro chloric acid be present on gastric analysis The ach lorhydria has been a most important factor in the final solution of the origin of the disease Addison and Biermer knew nothing about achlorhydria

How did it become recognized that this was a necessary part of the symptom complex? Test meals were not done until relatively late in clinical medi cine Cahn and von Mering[19] first studied the acid in healthy and diseased stomachs in 1886 During the next ten years many articles on the subject appeared in England on the Continent, and in this country It was soon noted by numerous investigators that when no free hydrochloric acid was found the patients were frequently anemic and that the anemia belonged in the group already designated as pernicious As late as 1900 however Faber and Bloch[0] could collect only 33 cases of pernicious anemia on whom a test meal had been done Martius and von Lubarsch[21] in the first monograph on achylia gastrica in 1897, re ported both pernicious anemia and secondary anemia associated with achlorhydria Achlorhydria was not then considered as a necessary part of the clinical pic ture The first large group of patients with perni cious anemia on whom test meals had been done were reported by Levine and Ladd[22] in 1921 In 107 patients only three were found to have free acid In two of these three patients the diagnosis was ques tioned In the light of present day knowledge all would be questioned One for instance, had had sev

mia and emphasizes the large size of the red cells and the increased color index The decrease in number of red cells the increase in size, and the increase in hemoglobin content were thus established very early as characteristic findings

Earlier workers used the red cell diameter as a measure of size With the development of the hematocrit the cell volume was found increased also and a more sensitive indicator of macrocytosis Capps[18] in his work on volume index found this always increased in pernicious anemia In our series of 579 patients all showed a macrocytosis if untreated except in the rare instance with a coincident iron deficiency Other clinical conditions will also produce a macrocytosis but seldom so marked as in a pernicious anemia Examples are liver disease, intestinal obstruction and nutritional deficiency such as sprue Ehrlich considered the presence of megaloblasts in the peripheral blood as diagnostic of pernicious anemia He insisted that these were pathologic nucleated red cells and not simply very young cells Although Ehrlich and others believed that the diagnosis of pernicious anemia should not be made without the finding of megaloblasts in the blood this view is no longer held A diagnosis should never be made of untreated idiopathic pernicious anemia in the absence of a macrocytosis of the red cells

The presence of an achlorhydria refractory to histamine stimulation is an essential finding All clinicians now accept the fact that idiopathic pernicious

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eral operations and a persistent diarrhea following an intestinal resection This patient probably had a symptomless obstruction of the small bowel with a macrocytic anemia Recently Goldhamer[23] in a report on the gastric acidity during remission in pernicious anemia, mentions 1 000 patients at the Simpson Memorial Institute as having had a test meal without finding free hydrochloric acid in a single one In our series of 579 patients a test meal was done in 546 Free acid was found but once This patient had a typical clinical and blood picture of pernicious anemia with subacute combined sclerosis A technical error was not excluded The test meal was not repeated because the patient died soon after the original examination No special studies were done to exclude other causes for a macrocytic anemia Recently we have studied two patients with a macrocytic anemia and a normal gastric analysis Both were found to have a benign chronic intestinal obstruction These two patients also had signs of a subacute combined sclerosis

A possible relation of the stomach to pernicious anemia through impaired nutrition was recognized long before test meals were done Immerman[10] in 1877 described pernicious anemia as a disease of nutrition due to faulty absorption of food Austin Flint[4] in 1860 said Nor is it difficult to see how fatal anemia must follow an amount of degenerative disease reducing the amount of gastric juice so that the assimilation of food is rendered wholly inade

quate to the wants of the body The English physician, Samuel Fenwick, especially emphasized this point of view His book, Atrophy of the Stomach, [25] was published in 1880 Here he recognized severe anemia as occurring with atrophy of the stomach In Chapter 3 on The Relation of Gastric Atrophy to Other Forms of Idiopathic Anemia he remarked that the cases of atrophy of the stomach with anemia reported by him were identical with those described by Addison as idiopathic or pernicious anemia He quoted Addison s description to emphasize the similarity Fenwick thought however that the anemia was produced by interference with nutrition He pointed out that the digestive powers of the stomach were so impaired that the usual post mortem digestion solution of the gastric mucosa did not even take place unless acid were added and the gastric contents would not digest egg albumin These observations of Fenwick are most important in the light of present knowledge of the relation of the stomach to pernicious anemia This atrophic condition of the gastric mucosa in pernicious anemia can now be verified in life by gastroscopy

William Hunter[26] long emphasized the relation of the digestive tract to pernicious anemia He considered the gastric atrophy as resulting from a gastritis due to swallowing bacteria and the characteristic glossitis to be produced by a specific microorganism He believed that a toxin of bacterial origin

in the intestinal tract was absorbed into the portal blood and destroyed red cells

The earlier students of pernicious anemia did not recognize central nervous system involvement In 1887, Lichtheim[27] described three patients with severe anemia and involvement of the central nervous system Lichtenstein [3] in 1884 had previously described cases of pernicious anemia with findings suggesting tabes dorsalis We now think these patients had pernicious anemia with subacute combined sclerosis In 1892, Minnich[29] described two patients with pernicious anemia who had serious cord involvement and studied the cord at autopsy He found changes especially in the posterior columns of the spinal cord In this country Dana[30] in 1891, in a discussion of degenerative diseases of the spinal cord, described a case with extreme anemia and diarrhea which was evidently pernicious anemia with cord involvement In the same year Putnam[31] described eight patients with combined sclerosis which we recognize as having pernicious anemia from the characteristic anemia and other symptoms It is interesting that few of the early observers did blood counts on their patients so the anemia was evidently quite extreme to be recognized only by pallor or weakness These observers continually emphasized that the nerve involvement is due to poor nutrition resulting from the anemia After 1890 following such early reports numerous articles appeared describing cord lesions In 1902 McCrae[32] reported fifty patients with pernicious ane

mia from the Johns Hopkins Hospital and found neurologic manifestations in twenty of these In 1900 Frank Billings[33] took as his subject for the Shattuck Lecture in Boston The Changes in the Spinal Cord and Medulla in Pernicious Anemia He emphasized the now well established relation of diffuse cord degeneration and pernicious anemia He thought the anemia and cord changes resulted from a simple toxin which was probably of intestinal origin His article is illustrated with many sections of spinal cord obtained at autopsy

Russell Batten and Collier[34] in 1900 in discussing subacute combined degeneration of spinal cord described this condition as occurring in patients with severe anemia which was evidently pernicious anemia They thought there was no etiologic relation of the anemia to cord changes In the earlier articles there is necessarily much confusion since the criteria for the diagnosis were not clear Many diagnoses were missed and often cases of severe anemia due to other causes were called pernicious anemia

The central nervous system is affected in 80 85 per cent of cases of true pernicious anemia The most common evidence of cord involvement is a diminution of vibratory sense The cord lesion may be the only significant manifestation of the disease it may be more serious than the anemia There is no parallel between the degree of anemia and involvement of the central nervous system Subacute combined sclerosis may arise from other causes The cord lesions usually

respond at least partially to liver therapy Sometimes the damage to the central nervous system is beyond repair so neurologic symptoms and signs may persist when the anemia is entirely relieved

The proof of the relation of the stomach to the origin of pernicious anemia is a most important discovery It is easy to see how the stomach was early incriminated since the anemia had been conceived of as a wasting disease due to impaired nutrition This was well expressed by Austin Flint[24] in 1860 as already quoted Immerman s classification of pernicious anemia as a disease of nutrition and Fenwick s work begun in 1871 on gastric atrophy as a cause of anemia have already been mentioned Henry and Osler[3] in 1886 described a case of pernicious anemia as due to gastric atrophy Numerous other clinicians made similar reports Pepper [11] in his very complete article however lays no emphasis on changes in the stomach Then, as gastric analyses were more widely employed came the discovery that patients with pernicious anemia had an achlorhydria and finally the conclusion of all clinicians that achlorhydria is invariable in the idiopathic form of the disease Achlorhydra usually if not always precedes the development of the anemia by many years and persists even in complete remissions Free hydrochloric acid is not only absent in idiopathic pernicious anemia but the amount of gastric secretion is greatly decreased Askey[38] has recently reviewed 47 cases of pernicious anemia reported as showing free hydrochloric acid

on gastric analysis He emphasized that none can be considered true Addisonian pernicious anemia by present-day criteria

What is the relation of achlorhydria to the causation of pernicious anemia? We are indebted to Castle[37,38] for the proof that achylia gastrica is a necessary link in the development of the nutritional deficiency producing the disease He showed that a patient fails to secrete in the stomach some unknown substance probably a ferment which acts on the food to produce a substance or substances necessary for the maturation of the red cells in the bone marrow and for the normal metabolism of nervous tissue The proof is simple Ground beef partially digested in the stomach of a normal man with normal gastric secretion when fed to a patient with active pernicious anemia initiates a remission and causes active blood formation as shown by a rise in reticulocytes and increase in red cells and hemoglobin Similar preparations exposed to digestion in the stomach of a person with pernicious anemia cause no reticulocytosis or erythrocytosis in other patients suffering from pernicious anemia to whom the material is fed Such observations proved that a substance supplied by gastric mucosa is a necessary link in the protection against pernicious anemia It was also shown that the achlorhydria by itself is not a factor but the ferment is never absent if free hydrochloric acid is present On the other hand the specific ferment may be present if free hydrochloric acid be absent Castle s work fur

nished the final proof that pernicious anemia is a deficiency dependent primarily on a gastric defect Many workers such as Austin Flint, were right in considering the absence of normal gastric digestion as a cause of anemia though they never thought of such specific action as that demonstrated by Castle Pernicious anemia may follow total gastrectomy Meulengracht[39] thinks Brunner s glands in the duo denum supply the specific ferment also If true this explains normal blood formation after some cases of gastrectomy

Castle s work disproved other theories of perni cious anemia Gastrointestinal toxemia infection and other possible causes are no longer mentioned The disease becomes a negative one due to the lack of something and not a hemolytic one, due to the action of some positive toxic agent

The discovery of a specific treatment for perni cious anemia is the most dramatic episode in the long history of this serious disease Many different meth ods of treatment had been used prior to 1926—iron hydrochloric acid arsenic transfusion splenectomy removal of infection special diets and drainage of the intestinal tract At times any method of treatment seemed to produce a remission Sometimes the effect of transfusion was life saving by initiating a remis sion No treatment however could be depended on to stay permanently the course of the anemia It was almost always progressive and usually ended in

death from anemia unless some intercurrent fatal disease developed

In 1920 Whipple[40] and his associates had begun a systematic study of the effect of different methods of treatment especially food and drugs on experimental hemorrhagic anemia in the dog They found that the most valuable agent in ameliorating the anemia was whole liver Other foods such as red meat had a similar effect to a varying degree but the effect was not so striking as with liver While Whipple was working with hemorrhagic anemia he emphasized in 1925[41] that even in complex anemia such as pernicious anemia anemia with nephritis and cancer cachexia food factors deserve serious consideration in the clinical management of the blood conditions Whipple did not apply his discoveries to clinical medicine however It remained for Minot and Murphy to find in a routine trial of liver in various types of anemias that the response in pernicious anemia was strikingly different from that in other types of anemia They were helped by the knowledge that the level of reticulocytes is an ideal method of gauging response to treatment Minot and Murphy s discovery was first announced in 1926 and was rapidly verified by clinicians everywhere

Liver and liver extracts affect the stroma of erythrocytes only This verified Whipple s idea expressed in 1922[42] that there is a scarcity of stroma building material in pernicious anemia With adequate liver therapy the blood of a patient about to

die rapidly responds and returns completely to nor mal The glossitis and other gastrointestinal symp toms disappear entirely The neurologic symptoms become improved or do not progress at times they disappear entirely There is nothing more dramatic in medicine than the effect of liver therapy on a pa tient with pernicious anemia Only the use of sulfa drugs and other antibiotics such as penicillin afford such brilliant results

It was soon found that a liver extract acted just as well as whole liver Extracts have been improved un til now these are almost perfect in their action A monthly injection of a potent extract will keep the blood normal and prevent the development of a neurologic lesion An extract of normal gastric mu cosa has a similar action as one would expect from Castle s discovery

Many attempts have been made to isolate from liver and liver extract a single specific substance re sponsible for the beneficial effect While highly con centrated preparations have been made no single sub stance has been isolated In the meantime a single chemical substance has been found which gives a specific blood response in pernicious anemia and re lated macrocytic anemias Folic acid a substance found in liver yeast spinach and grasses has proved to be necessary for the growth of certain bacteria and to relieve the anemia developing in certain vitamin deficient diets This substance was found to be effec

tive in macrocytic anemias due to a deficiency such as sprue, and other related conditions

Folic acid is a single chemical compound (pteroylglutamic acid) which causes a specific response also in pernicious anemia It matures the megaloblasts of the bone marrow so that the blood returns to normal It probably has little effect on the cord lesion The latest reports indicate a cord lesion may even develop while the anemia is disappearing and the blood count is normal

With folic acid the reticulocyte response is not so pronounced as with a potent liver extract but the full effect is excellent and the blood will return to normal No secondary reticulocytosis occurs in a patient treated with folic acid when liver extract is added The question is still unsettled whether liver extract and folic acid give a better result than liver extract alone Folic acid alone should never be used in the treatment of pernicious anemia since it is not the antineuritic factor It fails to prevent the development or progression of neurologic symptoms indicative of subacute combined sclerosis [43]

The anemia of pernicious anemia is due to the lack of a specific red cell maturating factor necessary for the normal development of the erythrocyte This may well be folic acid since the response of the anemia with adequate amounts of folic acid is complete The relation of liver extract to folic acid is now being investigated Liver extract contains small amounts of folic acid but not enough to explain its

anti anemic action Liver extract has a widespread effect on the individual needing it possibly through *its action on cellular metabolism, as shown by the* feeling of well being exhibited by a person with pernicious anemia after the treatment for a few days with liver extract The rapid clinical improvement is not due to a relief of the anemia It has been suggested that liver extract restores normal pteroylglutamic acid metabolism possibly by freeing it from its conjugate form in which it normally occurs in food stuffs According to this concept folic acid is related to the blood lesion only Further research may well *show that other specific substances necessary for nor*mal metabolism of nerve tissue are activated by liver extract Liver extract thus acts as an activator of cellular metabolism[44] rather than as furnishing specific substances preventing or relieving pernicious anemia This work suggests that a complex type of cellular enzyme disturbance exists in pernicious *anemia The action of liver principle in restoring* normal pteroylglutamic metabolism probably constitutes only one of its therapeutic effects

Summary

I have tried to review and clarify steps leading to our present knowledge of pernicious anemia as a clinical and etiologic entity The early history is most illuminating The development of the present concept of this complicated disease is a triumph of medical research Many great names both in clinical and

research fields are associated with the advance in knowledge of pernicious anemia Further research will almost certainly clarify problems still unsolved

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II

Some Functional Distresses in the Abdomen

Walter C Alvarez M D
1948



WALTER CLEMENT ALVAREZ

Walter Clement Alvarez was born in San Francisco in 1884 He obtained his M D degree from Cooper Medical College Stanford University in 1905 and studied at the Harvard Medical School in 1913 He practiced Internal Medicine in San Francisco from 1910 to 1925 and was a member of the faculty of the University of California School of Medicine from 1916 to 1926 when he joined the Mayo Clinic serving also as Associate Professor and after 1934 as Professor of Medicine at the University of Minnesota (Mayo Foundation) He has been president of the American Gastroenterological Association and editor of the *American Journal of Digestive Diseases, Modern Medicine Geriatrics,* and other periodicals Besides a large number of articles he has written *An Introduction to Gastroenterology* 1940 *Nervousness Indigestion and Pain* 1943 *The Neuroses* 1951 *Danger Signals* 1953

When a person complains of discomfort or pain in the abdomen the physician should remember that a survey of such patients made by Drs Rivers and Mendes Ferreira at the Mayo Clinic showed that one in four had a functional type of trouble

Flatulence

Flatulence is one of the commonest complaints of persons who have abdominal discomfort Usually they say they have gas, but a few questions show that they do not bloat and they do not pass excess amounts of flatus What they are troubled about is belching Then a question will usually show that the man is belching for twenty minutes or more at a time This always means that he is gulping the air and belching it out again This is a bad habit like cracking one s knuckles—it is a pure neurosis and at times a form of hysteria Often the cause is great fear or anxiety The man can stop his habit instantly if he makes up his mind to do it and accepts the doctor s statement that it is a habit Such persons do not need a diet and they seldom need much medicine except perhaps a sedative such as bro mural

A man who was belching loudly from bedtime until two in the morning would then fall asleep from sheer exhaustion I simply asked him What are you afraid of? And he said that he was facing bank ruptcy he was going to lose all of his life savings I

gave him a sedative to help him get sleep at night I told him to stop the belching, and he did

In cases of true flatulence the patient usually passes an unusual amount of gas from the bowel Sometimes his abdomen is bloated In many cases in which a hysterical woman gets to looking seven months pregnant, it is well to have a scout film made to see if the colon or small bowel contains an unusual amount of gas Practically always in these cases there is no extra gas in the bowel and the appearance of bloating is produced by the contractions of muscles back of the abdomen which push the abdominal contents forward In these cases the abdomen can suddenly go flat—especially after the injection of some morphine or the induction of anesthesia Usually in these cases the distention of the abdomen cames up gradually during the day and goes down at night

Some of these people suffer from pain in the abdomen and some at times vomit and look as if they were suffering from an intestinal obstruction Such persons generally get operated on several times to no purpose There is no diet or medicine that seems to help

Much flatulence is due to emotion Normally gas formed in the bowel is picked up by the blood and carried to the lungs where it is excreted Under the influence of pain or emotion the process is reversed and gas is taken from the blood vessels and put out into the bowel This process can take place rapidly

as when a urologist catheterizes the ureters The first scout film then taken will show no gas, while the one taken a few minutes later will show the bowel filled with gas

When emotion fills the bowel with gas, distention of the rectum if not quickly relieved will often bring on a mucous colic This will happen to a nervous girl when she goes out with a beau for the evening The distress can usually be blocked by the taking of some codeine and papaverine

Many persons suffer from much flatus when they are constipated and they get relief the minute they empty the rectum perhaps with an enema Apparently the presence of a plug of feces leads to a constant excretion of gas into the colon

Many persons will fill quickly with gas after eating some food to which they are allergically sensitive Others develop true flatulence when they have a cold or an attack of diarrhea

Nausea

Nausea can be due to worry, tension nervousness fatigue emotion or reverse peristalsis in the bowel It can be produced in some persons by the eating of fats which tend to reverse the waves in the stomach This symptom is rarely seen with disease of the upper part of the digestive tract such as a peptic ulcer or carcinoma of the stomach or cholecystitis It is seen occasionally in cases of beginning intestinal obstruction such as that due to carcinoma in the colon and particularly the sigmoid flexure

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Heartburn

I once studied a large group of persons who suf fered from heartburn, learning from them all I could about what seemed to bring their attacks and what gave them relief In diagnosing heartburn all one has to do is to ask the person to take his hand and show where the distress is Beginning over the epi gastrium the man moves his hand upward over the length of his sternum and sometimes even to the larynx The person who has the common type of burning in the epigastrium—a paraesthesia in the skin—does not move his hand away from the epigastrium

Much study of my patients and of the literature has left me with the conviction that heartburn is due usually to the regurgitation of gastric contents into an esophagus *which has been sensitized in some way* This element of sensitization is necessary because most persons who regurgitate mouthfuls of food do not suffer from heartburn It is not essential to the production of heartburn that the gastric contents be highly acid An interesting observation is that a woman may have very severe heartburn in one preg nancy and practically no heartburn in another and yet in both pregnancies she may have much regurgi tation of very acid gastric contents to the back of her mouth Evidently in one pregnancy her esopha gus became sensitized while in the other pregnancy it did not.

My researches indicated that heartburn is rarely

Nausea is commonly complained of by migrainous women, especially when they are tired In them it may take the place of a headache In some sensitive women, nausea may be a symptom of disgust Sometimes overworked executives will wake at midnight with nausea which will bother them for a couple of hours or so One can easily find out if this nausea is due purely to fatigue by sending the man on a vacation Usually then he starts sleeping all night comfortably

Occasionally nausea is due to a failing heart and in the case of many an elderly person, it is due to a small stroke Nausea is complained of by some nervous persons who have a psychotic inheritance In some cases it may originate in the brain or in the balancing mechanism in the ear It can be due to the eating of certain foods to which the person is allergic or otherwise sensitive Nausea of course, is a common symptom in pregnancy and sometimes during menstruation *I have seen nausea as the only* symptom of too much smoking or chewing of tobacco

Nausea is a very difficult symptom to relieve but nowadays Bonamine or Dramamine may help Sometimes the taking of solid food will drive the waves in the intestine downward again and with this there will come relief from nausea In the presence of constipation an enema may stop nausea instantly In some cases lying on the right side will relieve nausea

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My researches indicated that heartburn is rarely

due to any organic disease Often there is a hereditary tendency to it in a family One man said that his six brothers and his father all had heartburn There is a strong tendency to it in many Jewish families Curiously, a number of persons who suffered from ulcer told me that when they had their hunger pain they had no heartburn, and when they had heartburn they had no ulcer pain The commonest causes of a spell were eating too much eating certain things drinking certain liquors, smoking too much smoking a certain brand of tobacco, or getting angry Several men said that when they lost their temper they were on fire for four days Many said that they didn t know why spells came or why as suddenly they went away

The patients said that the best thing they ever found to relieve heartburn was the drinking of half a glass of water in which a half teaspoonful of sodium bicarbonate had been dissolved A tablet of some antiacid is much less likely to work because it gets neutralized in the stomach and has no effect on the esophagus

The importance of recognizing heartburn is that it is sometimes confused with the pain of angina pectoris of gallstones or of an ulcer Often the distress of heartburn is associated with a rending feeling in the thorax

Regurgitation

Quite a number of persons complain of epigastric distress which is relieved by the regurgitation of

food The physician must differentiate between re gurgitation and vomiting they are two different phenomena Vomiting is a complicated act involving contractions of voluntary muscles Regurgitation is produced only by waves running up from the bowel through the stomach and up the esophagus With this there rarely is any nausea and there is never any retching Regurgitation often starts even before the meal is finished As the patients say they boil over as a baby does The process often goes on for hours *Sometimes the symptom comes in spells*

In the worst cases regurgitation wrecks the per son s social life because he (or she) cannot eat with other people A few persons can hold the regurgi tating waves down if they have to But all of them say they prefer to let the food come up because then they get relief from a pain or distress in the epigas trium Some regurgitators ruminate—in other words they swallow the food again

The tendency to regurgitation and rumination runs in families The symptom usually is seen in women but it appears occasionally in men who are usually nervous and often frail looking and not too masculine

In a series of cases studied by me the patients all had psychotic alcoholic or epileptic relatives Hence the disease appeared to be an equivalent of psychosis Many of the schizoid women who suffer at times from anorexia nervosa regurgitate what little they eat Some of the women who have a lifelong tendency to

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regurgitate get spells whenever they are tired, angry excited, tense, worried, or unhappy Normal women may regurgitate only when they are pregnant or, more rarely when they are menstruating or when they are constipated These conditions all tend to reverse the ripples running along the digestive tract

The surgeon should remember that regurgita tion is always functional in nature In my fifty years of practice I can remember only two cases in which it was associated with organic disease in the abdo men One of the patients had a duodenal ulcer and the other had gallstones Both were operated on suc cessfully, but in neither case did this relieve the regurgitation I have known a few mildly psychotic women who had had five or six futile operations per formed for regurgitation

I know of no good treatment which helps An occasional patient who is badly constipated can be helped by a daily enema which lessens the tendency to reverse rippling in the bowel I have seen a few persons who regurgitated mainly or only, a food to which they were allergically sensitive

Functional Types of Vomiting

There are some highly nervous or mildly psy chotic persons who vomit easily and under slight provocation They can vomit under either startling or unpleasant circumstances Migrainous and hys terical women can vomit easily Nervous children can vomit whenever there is an excitement such as a school picnic, a graduation or the start of a journey

Many nervous men and women vomit only their breakfast On studying a group of these persons, I found that all of them had psychotic relatives Evidently the symptom can be an equivalent of psychosis As with regurgitation so also with vomiting the patients prefer to vomit rather than put up with the abdominal discomfort that follows an effort to hold the food down

Some of the patients can be helped with rest and sedatives They must be encouraged to make an effort to restrain vomiting when the impulse comes

The Sore Colon, or Mucous Colics, or 'Spastic Colitis'

I hate the terms mucous or spastic colitis because in these conditions there is no colitis The bowel is normal and the symptoms are due only to nerves playing tricks with it It is unwise and unfair to tell a patient that the X ray examination showed a diseased colon It is much better to say Your colon is normal It is much better for the patient to know that her troubles are not due to any serious disease but to a nervous inheritance or some fatigue or psychic strain

Many persons who camplain of diarrhea really do not have it If asked what they pass from the bowel they will say that it is only gas with a little water and brown mucus This means that they have had a mucous colic During such a colic the bowels do not move and the giving of an enema will show that the lower half of the bowel is empty Perhaps

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and not in the cavity can be shown often by picking up a fold of skin and subcutaneous fat and pinching it On one side of the abdomen this maneuver may produce pain but on the other side it may cause no distress

Occasionally, a pain in the abdominal wall follows the distribution of a spinal nerve Then one must suspect a tumor in the spinal canal or marked arthritis around a certain joint, or a diseased or displaced disc

Many a person who is told that he has a peptic ulcer really has only an arthritis of the little joint that lies between the main part of the sternum and its xiphoid process In some persons and at times this joint becomes so tender that any pressure on it causes pain and then the diagnosis is easy A similar pain can be produced by arthritis in the two joints around the tip of the tenth rib

In cases like this one will often find on pressing on the ribs or on the intercostal muscles that the patient s distress is due to a periostitis or perichondritis Many an arthritic woman who thinks she has a cancer of the breast really has only a short section of rib that is sore to the touch

Pseudo Ulcer

There are many persons with no sign of ulcer even at an operation who for much of their lives have suffered from fairly typical hunger pain which is relieved by eating It rarely bothers the patient at night and it is rarely followed by complications

spasm is holding the fecal matter back in the ascend ing colon

Constipation and Distresses It Can Produce

Few physicians seem to know that in a few sensi tive persons, flatulence abdominal discomfort hun ger pain, tendencies to regurgitate or to burp,' or to have hiccups can be produced by constipation Often this is not recognized because the person is having one or more small bowel movements a day But these are not large enough and hence leave in the lower end of the bowel a plug of feces In highly sensitive persons this plug tends to give off ripples which on reaching the duodenum stomach or esophagus produce distresses of several types The minute the person empties the rectum and sigmoid colon with an enema he has relief Gas will stop forming and distress around the cardia will disap pear Obviously a person can easily find out if his abdominal distress is due to a hidden constipation All he has to do is to take an enema every day for a few days

Abdominal Distress Due to Arthritis of the Spine or Fibrositis of the Abdominal Wall

Many persons who complain of abdominal dis tress are suffering from arthritic pain referred out from the spine others have a fibrositis involving the tissues of the abdominal wall One can often suspect this when they have the same type of distress in the chest wall That the abdominal distress is in the wall

and not in the cavity can be shown often by picking up a fold of skin and subcutaneous fat and pinching it On one side of the abdomen this maneuver may produce pain, but on the other side it may cause no distress

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Pseudo-Ulcer

There are many persons with no sign of ulcer even at an operation who for much of their lives have suffered from fairly typical hunger pain which is relieved by eating It rarely bothers the patient at night and it is rarely followed by complications

These persons have what I call pseudo ulcer It has been described by a number of physicians and one man in Germany wrote a whole book on it

The syndrome can be produced in sensitive persons by the eating of some food to which the victim is allergically sensitive In my own case, I used to produce it by eating eggs In some persons it can be produced by constipation, in others by a cold I have seen it clear up the day a woman with a chronic inflammation of an antrum had the cavity drained by the making of a little window into her nose A few persons can get hunger pain by sitting hunched over so that a fold of abdominal wall presses on the duodenum Highly irritable carriers of epilepsy (without spells) can suffer from hunger pain My experience indicates that persons with pseudo ulcer rarely develop ulcer in later years When they do I suspect the roentgenologist missed demonstrating an ulcer during the early examinations

It is well that a physician should know that this disease exists so that he will not be too distrustful when roentgenologists report a normal duodenal cap

Food Sensitivity and Food Allergy

A considerable number of persons suffer from flatulence and abdominal pain which is due to the eating of some food to which they are highly sensitive It is a good idea when a person is constantly suffering from abdominal gas colic or perhaps slight diarrhea to have him live for a *couple of days*

on *only* oatmeal and butter and sugar for breakfast with a broiled lamp chop and some rice for luncheon and supper and a canned pear for dessert On the rice he can put butter and sugar Nothing else is eaten or drunk for forty eight hours If this does not give relief the distress is probably not due to food sensitiveness If the person is having spells of pain and distress once a week or so he should keep a record of the unusal foods eaten just before an attack to see if any particular one is responsible for every spell

If a person is having a bad spell only once a month or six weeks the chances are great that his trouble is not due to sensitiveness to a food If it were the food would have to be one rarely eaten and then the person would quickly identify it

If a person comes to suspect that a certain food is responsible he should stop eating it Then if it was responsible for his distress this should imme diately disappear If he does not get relief in forty eight hours, his guess has been wrong

Skin tests are rarely of value when it comes to trying to find out what foods are causing trouble One should never depend on them When I see a person who for months has deprived himself of some food simply because his skin once reacted to it I ask him to go out and eat heavily of that food Usually he returns to say that the experiment made him no worse—which shows that the skin reaction was deceiving

Abdominal Pain Associated with Migraine

On reviewing the records of hundreds of mi grainous patients I found that many of them suffer distress or a pain in the upper right quadrant of the abdomen That this was not due to disease of the gall bladder was shown by X ray studies, and in several cases by the persistence of the pain after the re moval by the home surgeon of a stoneless gallbladder There is no question then that many migrainous women suffer from a functional type of pain in this region

There are a few migrainous persons who under great excitement or when angry can go into what looks like an attack of intestinal obstruction or a gas tric crisis with much painful retching Women with such attacks sometimes get operated on several times without result

Abdominal Pain of Gastric Crisis Type

The consulting internist will see every year pa tients who have what looks like a gastric crisis of tabes but who show no signs of nerve syphilis Usu ally such a person has been operated on more than once and has parted with his appendix and gall bladder These persons have more vomiting than should go with inflammation of any abdominal organ and they do not quiet down perfectly with morphine During a spell the abdomen is soft there is no fever and the leucocyte count remains low If nothing is done the patient recovers in a day or two

The diagnosis is easy if the person has had many such spells that all cleared up

I have found such spells in migrainous persons or in children of highly migrainous parents in carriers of epilepsy and in relatives of the psychotic Many psychotic persons complain primarily of an abdominal misery or of abdominal pain On questioning them carefully, one often finds that their attacks of abdominal pain and perhaps diarrhea come when they go into a panic fearing that they are going insane like a mother or an aunt

Always when a patient complains of many spells of abdominal pain which were not relieved by four or five operations the physician will do well to ask about psychotic or epileptic or alcoholic relatives

Abdominal Pain Due to a Tantrum of Temper or Some Excitement

I have seen cases in which attacks of abdominal pain and vomiting were due purely to a tantrum of temper or to eating when the person was much fatigued or distressed by something like testifying in a court trial I remember a man who on four occasions had had his abdomen opened to no purpose His wife said that every time he had had a tantrum of temper Another man nearly got operated on for supposed intestinal obstruction He had eaten after a very distressing experience in a court trial Still another man an army officer got operated on needlessly when he developed severe abdominal pain His

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III

Infections in Cardiovascular Disease

John T King M D
1949

trouble was that he ate after having been forced to *testify at a court martial against one of his friends*

Abdominal Distress Due to a Little Stroke

Every year I see a number of older persons with abdominal distress or pain who have been thoroughly examined by physicians expecting to find a cancer of the stomach or bowel On questioning these persons, I got a history of a little stroke that came suddenly on a certain day with perhaps some dizziness or partial loss of the sense of balance It was followed by a change in character, some loss of memory an increased irritability, and *perhaps some difficulty* in writing In such persons the abdominal distress was due to some sort of nervous storm referred out from the injured brain Usually the distress cleared up in a couple of months

OUR honored guest Dr Bohan would I think support me in the view that one of the pleasant prerogatives of accruing years is the privilege of wag ging one s head at youth and speaking if not wisely at least from experience I welcome tonight s oppor tunity to deviate slightly from standard deviations and controlled experiments and to gather together some loose ends of things reported and things ob served The basic concepts to be discussed have been forced upon me insistently since I first began to take case histories and examine patients I think you will find that Dr Bohan has had the same experience I am referring to the repeated observation that certain infections seem to characterize the life histories of our patients with degenerative cardiovascular dis eases Thus I who claim the distinction of being most honored guest in being selected to give this lec ture and Dr Bohan to whom I give the place of next most honored guest meet in a common heresy For in spite of considerable evidence on our side our views are not yet generally held Dr Bohan[1] has gone more broadly into this relationship (of infection to disease) and has made some very pertinent observa tions on the important role of dental sepsis My ex perience in this particular is too limited to be worth reporting If I can escape pertinent infection I hope to live long enough to follow the direction to which he has pointed



John T King

John Theodore King was born in 1889 in Baltimore Maryland He obtained his A B degree from Princeton University in 1910 and his M D degree from Johns Hopkins University in 1914 In 1917 he joined the faculty of the Johns Hopkins School of Medicine and from 1925 to 1933 was Assistant Visiting Physician at Johns Hopkins Hospital He has been president of the Baltimore City Medical Society and of the American Clinical and Climatological Association He is the author (with J C Bramwell) of *Cardiology* 1942

certain infections that have been noticeable in my histories of coronary artery and hypertension cases for many years These are the diseases classified as indicative of the rheumatic state —rheumatic fever chorea and growing pains—and repeated tonsillitis quinsy or streptococcal pharyngitis Typhoid fever has been found to cause coronary arteritis and has been suspected of predisposing to hypertension but this infection is so rare that it is fast disappearing from case histories except in the highest decades of life Occasionally malarial parasites migrate into the coronary vessels and induce obstruction Diphtheria may damage the conduction system I have never read or observed any cardiac sequelae from the usual childhood diseases—measles mumps and pertussis Scarlet fever may be in a different category Some English writers seem to accept this streptococcal disease as sufficient etiology for the establishment of rheumatic valvulitis Whether this is true or whether scarlet fever and the rheumatic state (possibly not recognized) both afflict certain individuals I cannot say I have no data on the relation of scarlet fever as such to subsequent cardiovascular disease but the infections that seem to me to constitute the nearest approach to a common denominator in coronary disease and hypertension are the other streptococcal or para streptococcal diseases

I have never had a theory as regards these infections and did not become interested in them as etiologic agents until I noticed that I could almost

A man of sixty who consults a physician is not merely an individual who works more or less assiduously, who may or may not smoke who plays nine or thirty six holes of golf or who may be suffering from a frustration or from subconscious rage I prefer to think of him as a person who has suffered the slings and arrows of outrageous fortune for sixty years, with the constitution God gave him and in the environment in which fortune placed him In other words, he is the end product of a variety of influences that determine whether he is to be sound or feeble at sixty whether he is to have a good heart and normal blood pressure or hypertension or coronary disease One of the great deficiencies it seems to me, in much of the research on cardiovascular disease is that the sixty years through which our hypothetical patient has passed are largely ignored and the cause of his breakdown is sought diligently through X rays electrocardiograms blood chemical studies search for vasospastic substances or abnormal hormone secretions and psychoanalysis on the assumption that the cause is still operating and is susceptible of discovery In some cases such search proves fruitful in all too many it is rather like subjecting the city of Berlin to a careful study by architects and surveyors to determine why the houses are no longer fine upstanding structures

Tonight I wish to discuss not all of the possible factors that may be instrumental in bringing on degenerative changes in the cardiovascular system but

events is as follows The patient usually but by no means always a child, is subject to upper respiratory infections The next step is probably the experience of that mild manifestation of rheumatic infection commonly known as growing pains or the development of frank rheumatic fever In our part of the country, where frankly hot and swollen joints are not seen often in patients with the rheumatic state *the subject I think* is more likely to complain of growing pains than of rheumatic fever I should like to know what proportion of patients with rheumatic valvulitis give a history of growing pains only as compared with a story of frank rheumatic fever In England growing pains are rather ignored but in this country they are generally considered I think a *mild manifestation of the rheumatic state hence* a point of history worthy of being recorded Many patients, when asked about this experience look puzzled and wonder how they could be expected to remember such an insignificant event and smile tolerantly at the questioner Others reply promptly and emphatically that they recall these pains usually in *the legs, as if they had occurred yesterday—and this* in some cases after the lapse of many years Then come rheumatic carditis tonsillitis the rheumatic state and rheumatic disease of the heart in that sequence It is doubtful whether any person with rheumatic fever escapes some infiltration of the myocardium with Aschoff bodies and the endocardium and pericardium are commonly affected The patient

tell in advance the kind of story that could be expected from a patient with arteriosclerotic heart disease or hypertension Except for the fact that frank rheumatic fever is less often reported, the case history of such a patient is quite similar to that of the patient with rheumatic valve disease "I had tonsillitis every year or two, until I had them removed at the age of eighteen Since then I have had very little trouble—only one streptococcal sore throat ' I had sore throat as a child every few weeks during the winter and lost a good deal of time from school I was advised to have them removed but the doctor did not insist and after I grew up the attacks ceased troubling me I had my tonsils removed when I was young do not know exactly why I had growing pains when I was about fourteen remember them well Similar stories and variations thereof became so familiar early in my practice that I have never ceased to take a careful history along pertinent lines One might not be impressed by the importance of these infections if he approached every patient after some one else had taken the history my interest arose from taking my own histories *Whether the incidence of the infections under study is much higher in cardiovascular cases than in cases of other diseases will be considered later*

Meanwhile what do we know, or what is generally believed about the etiology of the non *syphilitic acquired cardiovascular diseases? None of* us I suppose seriously doubts that the train of

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may escape without permanent damage that we can find or he may develop pericardial adhesions disturbances of cardiac conduction, perivascular fibrosis, or a recognizable valve lesion Parenthetically, I might say that calcific aortic stenosis now generally believed to be allied to the rheumatic infection but in which only a minority of histories positive for rheumatic fever is obtained now constitutes a major item in my personal diagnostic file Christian, Sosman, Karsner and others have developed a large new field of knowledge and aortic stenosis seems to be outstripping mitral disease in my patients though many of course have lesions of both valves

A patient whose history throws some light on both growing pains and calcific aortic stenosis consulted me last week He was 82 years of age and was suffering from heart failure of recent onset He gave no history of tonsillitis or rheumatic fever He insisted he had always been healthy The only positive feature of his story was the recollection of growing pains He was quite clear about this and said they had been felt in the legs Examination showed a frank picture of calcific aortic stenosis with insufficiency in the absence of syphilis this picture could probably have resulted only from the rheumatic infection—in this case camouflaged as growing pains Also a 61 year-old man whom I saw last Thursday may be of interest He was a Jew (of a race notably liable to coronary disease as Osler pointed out) and was also a typical driving business executive until his

retirement four years ago But let us delve deeper I found he had had frequent tonsillitis prior to tonsillectomy twenty years ago Also he recalled having growing pains as a boy At the age of 57 he had a posterior coronary occlusion followed by symptoms of coronary insufficiency At the last examination the blood pressure was 188/96 the heart slightly enlarged electrocardiographic changes from the occlusion persisted On the same day a 46 year-old well adjusted housewife reported for examination She was slightly obese There was the same story of frequent tonsillitis and growing pains then tonsillectomy when she was about 17 years old Now she is having mild angina with electrocardiographic changes seen only after a Master s exercise test The examination was otherwise normal the pressure 160/97

Since every layer of the heart may be involved by rheumatic infections how do the coronary vessels fare? Some cases of coronary occlusion have been reported in the midst of rheumatic fever but this is probably uncommon In the recent war a medical officer observed ten young soldiers with clinical and electrocardiographic findings of coronary occlusion All had suffered recent upper respiratory infections all showed elevation of sedimentation four experienced joint symptoms six had none All recovered It is difficult to escape the conclusion that these men had coronary arteritis leading to occlusion based on a condition that we may call the rheumatic state

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concerned in the etiology of certain cases of coronary occlusion However, it can be shown that a history of frank rheumatic arthritis occurs in only a minority of any large group of cases of coronary occlusion I shall show its incidence shortly In the ten cases reported by Weinstein[2] from the army it was shown that severe throat infections occurred in all that all had coronary occlusions and that six had no joint symptoms What is the possible relation between the initial infection and consequent coronary disease? Moreover if a single severe throat infection can cause a coronary occlusion what is the fate of the person who has tonsillitis numerous times even though he may seem to suffer no serious consequences at the time?

Those of you have read the work on the pathogenesis of atheromatous lesions by Winternitz and his associates[3] will recall that they concluded that some infection was concerned in the lesions that they appeared to be reactions of inflammation hence probably preventable to some degree What kind of infection could be responsible? Hardly the ordinary childhood diseases or the common cold almost certainly not syphilis and typhoid fever and pneumonia are probably too uncommon to be important The rheumatic state seems to stand out as the most likely culprit but only in certain cases Is there a possibility that something that may be called the rheumatic state to all intents and purposes may occur in the absence of frank joint symptoms? Work

although a majority had no joint manifestations At Walter Reed General Hospital a large number of cases of coronary occlusion were studied The young est who came to my attention was a powerful soldier of 21 years One year previously he had had rheu matic fever He recovered, was inducted, and was assigned to driving a truck Under our observation he passed through an attack of typical coronary oc clusion Here again it seems reasonable to suppose that the occlusion was induced by a coronary arte ritis since such a reaction to the rheumatic infection is now well known to pathologists Or take the case of a private patient a professor in a country college a man of leisurely activities and exemplary habits who had escaped the wear and tear of modern life to a large degree While visiting in Baltimore at the age of 44 he had a coronary occlusion His story re vealed that he had had rheumatic fever ten years before as well as the throat infections that commonly precede it Such cases are seen often enough to lend weight to the conclusion that the rheumatic state can and does induce in certain patients a coronary arteritis leading to a subsequent occlusion However, when the interval between the infection and its re sult goes beyond a few months or years it seems to be a part of human nature to ignore the connection between the two occurrences in spite of the improb ability that an atheromatous plaque whenever in curred will ever resolve Thus there is evidence that the rheumatic state loosely defined, is probably

joint symptoms—to be quantitative only They believed that all these twenty two patients had similar tissue damage—that characteristic of rheumatic fever Some authors have used the term streptococcosis to designate the lingering disease that may follow acute hemolytic streptococcus infection The facts now seem to justify the conclusion that streptococcosis and rheumatic fever are the same sort of disease and that the patient who reacts with frank joint involvement is merely somewhat sicker than the one who escapes this symptom Any physician of experience has seen many cases of non syphilitic valvulitis of the heart in which there was no history of antecedent joint symptoms

So it seems established beyond reasonable doubt that a rheumatic state follows various streptococcal infections joint involvement or no joint involvement also that such rheumatic state may affect the myocardium whether joints are inflamed or not In discussing the etiology of coronary occlusion we should I suppose take the view that this is an arterial rather than a cardiac problem Inflammatory reaction to the rheumatic state in the arteries is now well known to pathologists The possible role of tonsillitis in the etiology of coronary disease has long interested me though this interest was aroused not on theoretical grounds but because of the repeated similarity of histories

The tables just shown you point to a relatively high incidence of rheumatic fever and excessive ton

carried on in the late war suggests that this may be the case Rantz Spink and Boisvert[4] reported that a non suppurative continuing disease often associated with electrocardiographic changes and with or without joint symptoms, followed a throat infection in more than one fourth of 200 soldiers who were studied in an epidemic of hemolytic streptococcus infection The carditis seemed to be more definite and persistent in those men who developed joint symptoms but, except for degree there seemed to be no important difference in the findings of those who had arthritis and those who did not A very similar lingering illness also with signs of carditis has been found to follow scarlet fever in a certain proportion of cases Again as a war contribution Watson, Rothbord and Swift reported a series of cases that seem identical with those of Rantz and his collaborators Of 110 patients with scarlet fever exactly one out of each five developed pronounced and unequivocal electrocardiographic changes comparable with those seen in active rheumatic carditis In three cases these findings were noted during the acute phase in nineteen they occurred during convalescence Elevation of temperature, leucocyte count and sedimentation of the erythrocytes were commonly observed Eight of the twenty two patients had clinical rheumatic fever four had transient and mild joint symptoms, seven had no signs of joint involvement The authors found the differences in the three groups—the frankly rheumatic the mildly rheumatic and the group without

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sillitis in the 140 cases of coronary occlusion as compared with the controls The 110 control cases were taken from my office files and were instances of no disease or of some such conditions as psychoneurosis carcinoma tuberculosis, syphilis, or some other condition in which the streptococcus is not under suspicion in an etiologic role The highest relative incidence of excessive tonsillitis occurred in the histories of the youngest patients Patients in this age group are probably not numerous enough to be reliable statistically Nevertheless the higher incidence of infections in the coronary group as compared with controls carries through to the highest decade recorded Histories are never completely reliable I have had several cases in which a completely negative throat history was given and in which I was able to observe typical acute follicular tonsillitis Other patients who gave positive histories may have had non streptococcal infections of the upper respiratory tract However the same criteria were observed in recording histories of coronary and control cases and the controls were selected so that they corresponded in age and sex with the coronary patients These figures were subjected to statistical analysis The ratio of observed difference to standard deviation of the difference was 2 8 making it very unlikely that these figures could occur by chance

By the time we see these patients damage has already been done Many have ceased having acute throat infections since they matured others have had

tonsillectomy performed before they consult us After coronary artery symptoms have developed, we can expect nothing from tonsillectomy except to retard the progress of arterial disease in those patients who continue to have acute infections

While I was collecting these data a patient consulted me who corresponded roughly with the hypothetical 60 year oldster referred to above Actually he was 59 years old an executive of a textile firm His father had died of cerebral hemorrhage at 59 his mother had passed 70 and died from valvular heart disease My patient had classical angina pectoris without complication except slight systolic hypertension This immediately suggests that two popular theses are correct—that cardiovascular disease is an hereditary disorder and that business executives are particularly vulnerable But what do we find on further probing? This patient had not only the usual childhood diseases but scarlet fever as well At about the age of 10 he had an obscure fever diagnosed as typhoid, though not verified in the laboratory I have encountered this story in other patients who later showed rheumatic stigmata—a history of fever diagnosed as typhoid at an age almost too early for this disease and I have thought that this picture was probably caused by rheumatic fever But we shall pass this episode as obscure He recalls definitely that he had growing pains in his teens and that they affected his legs He had repeated tonsillitis but did not have the tonsils removed until

twenty years before he consulted me This sort of story is so characteristic of patients with coronary artery disease that I have come to believe that hered ity is influential, not in a direct transmission of the condition but in determining an individual who is susceptible to the pertinent infections we have been discussing After all, we have a perfect parallel in the hereditary factor in tuberculosis

For the time being, let us leave our coronary problem and consider hypertension The two condi tions, as you have already found, I am sure, are close ly related The occurrence of hypertension in pa tients who suffer coronary occlusion and the evi dences of coronary disease in our patients who com plain primarily of hypertensive symptoms are too frequent to be due to coincidence alone I have found it impossible to obtain figures on the previous blood pressure readings of many patients with coronary disease and occlusion, as so many are seen only after the symptoms of occlusion set in However, reports by the patient himself in some cases, actual observa tions in others and the subsequent behavior of the pressure in still others make it clear that some degree of hypertension very often a moderate elevation pre cedes the occlusion in an impressive number of cases though by no means in all cases Yet there is no rea son to believe that the hypertension induces coronary disease and occlusion In this connection let me sug gest that in your consideration of the various prob lems evoked by hypertension you get your foot on

base and reason from a condition that causes a purely mechanical hypertension in arms and head over many years This condition is coarctation of the aorta and the hypertension in coarctation is a condition caused by obstruction of the aorta just beyond the arch but it is not a disease in the sense that usual types of hypertension are Thus, in coarctation the heart head and arms are exposed to heightened pressure from immediately after birth Yet autopsy reports show that while the coronary vessels are thick and muscular the intima is unchanged I have seen some twenty such cases with ages extending from about 12 to more than 50 years None showed any sign of coronary artery disease Moreover (and this will be pertinent to our discussion of the etiology of hypertension) these cases do not show the picture of diseased arterioles in the arms and ocular fundi such as we see in classical hypertension The increased pressure in coarctation causes aortic insufficiency and cerebral aneurysms in some cases yet the retinal arterioles while very tortuous are of good caliber and healthy appearance The hypertension that is found so often in coronary disease is of the usual variety and due to disease of the smaller vessels Thus there is the suggestion that coronary disease and small vessel (arteriolar) constriction are due to some common etiologic agent

Another valuable lesson that may be derived from coarctation is that hypertension *per se* does not cause heart failure In occasional instances an aortic in

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ducing hypertension but when both renal arteries were largely constructed a significant and permanent hypertension could be established So with arteriolar sclerosis hypertension seems to be related to con striction of the afferent arteriolar bed of the kidneys rather than with similar changes elsewhere in the body There are well known exceptions to this rule in conditions such as Cushing s syndrome pheo chromocytoma and coarctation In the absence of such exceptional causes the basic pathology of hyper tension tends to be localized somewhere along the urinary passages Constriction of the main renal arteries by arteriosclerosis small artery sclerosis acute and chronic glomerulonephritis pyelonephri tis ureteral stricture prostatic obstruction have all been related to arterial hypertension Thus in gen eral it seems likely that most cases of hypertension will find their explanation in obstruction of the flow of fluid somewhere between the renal arteries and the outside world Such clinical observations are quite compatible with the experimental findings of Goldblatt especially if we ignore the question of some vague vaso pressor substance and consider the elevation of blood pressure on a mechanical basis It seems to me that this matter of urinary flow resulting from blood flow to the kidneys has been somewhat neglected in the explanation of blood pressure The general doctrine is that blood pressure is maintained by the pumping action of the heart against a certain volume of blood against elastic blood vessels and end

sufficiency is induced by the increased pressure in the aorta, and the heart embarrassed thereby but angina pectoris or cardiac failure is conspicuously absent in coarctation This is in exact accord with an axiom of medical practice that, when a patient with hypertension develops symptoms of cardiac failure, then that patient has coronary disease as well as hypertension So, whether we see a patient with hypertension only or in the midst of a coronary occlusion we can be sure that the hypertensive individual (provided he does not have a coarctation) is quite likely to have diseased coronary arteries while *our patient with the coronary occlusion is very likely* to have had a chronic hypertension All this has led to the use of hypertensive cardiovascular disease to designate this combination of large and small artery sclerosis with its varied symptomatology

It now seems established beyond reasonable doubt that the essential pathologic lesion in the usual *type of hypertension lies in the small arteries of the* body but notably in those of the kidneys especially in the afferent arterioles just short of the glomeruli Such arteriolar narrowing is found in the other viscera in the skin and brain and evidences of it are to be viewed directly in the ocular fundi The essential lesion however as regards hypertension seems to be *that of the kidneys in this respect* we find an analogy with Goldblatt s experiments You will recall that *this worker* was able to compress various arteries of a size comparable with the renal arteries without in

nephritis represents the physiologic counterpart of the syringe experiment The healthy child forms and discharges urine in proportion to the amount of fluid taken in the blood pressure rides on an even keel He then has an acute sore throat most likely streptococcal then a hiatus followed by an extensive inflammatory reaction in the renal glomeruli then anuria edema rise of blood pressure establishment of urinary flow, and gradual recovery accompanied by fall of blood pressure to its previous level But if the kidneys do not return to normal—for example if glomerulonephritis becomes chronic or if arteriolar narrowing takes place then we are dealing with a persistent obstruction of the filtration system and pressure remains elevated

It is a time honored axiom that acute nephritis occurs as a slightly delayed reaction in the glomeruli to an infection the chief offender again is the strep tococcus whether in the form of scarlet fever or ordi nary tonsillitis or pharyngitis Thus we are dealing again with the type of infection dealt with already in our discussion of heart disease and the rheumatic state

However we find a quite different pathologic basis for acute nephritis from what is found in most cases of hypertension though the causes of the hyper tension in the two states may be separated by only microscopic distances—the distance from the incom ing arteriole to the glomerulus The basis of chronic or ordinary hypertension is in the narrowed afferent

resistance of the arterioles But, the neglected factor is the filtration system and system of pipes known as *the urologic tract This mechanism is capable of re* moving huge amounts of fluid from the blood and releasing it to the outside world If the blood pres sure falls too low the system ceases to function thus *conserving fluid if the blood pressure rises or the* circulation is accelerated the flow of urine increases Thus we have four factors in blood pressure—cardiac pumping action blood of a certain volume and vis cosity lateral and end resistance of the blood vessels and a sensitive filtration mechanism capable of regu lating the volume of fluid in the circulatory appara tus

Let us suppose that this filtration system becomes clogged Goldblatt s experiments clogged it acute and chronic glomerulonephritis clog it and the vari ous other lesions noted above also interfere with the normal flow of fluid to the outside of the body Affer ent arteriolar narrowing is in the same category I think of this problem as being analogous to a clini cal syringe the fluid in the syringe being the blood the piston representing the heart with its propulsive force and the needle representing the urologic pas sages So long as the needle is of a certain standard caliber and clean we can imagine that a certain pres sure will be created in the body of the syringe But if the needle becomes dirty or *partly obstructed from* any cause then a greater head of pressure is set up in the syringe all other forces being equal Acute

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renal arterioles This sclerosis may be widespread elsewhere in the body, though the sclerosis outside the kidneys may have no bearing on the level of blood pressure In other words there is a vascular disease of wide distribution Hence, it would not be surprising if a common etiology lay behind the two so frequently associated vascular diseases—large vessel sclerosis (leading in some cases to coronary insufficiency and occlusion) and small vessel disease

Fifteen years ago having been struck by the frequency with which patients with hypertension reported frequent and severe throat infections in the past I made a study of the backgrounds of 200 hypertensive patients This analysis included the number reporting an extraordinary frequency of attacks of tonsillitis or streptococcus sore throat the number upon whom tonsillectomy had been done and the number showing tonsil infection when examined, also those with rheumatic valve disease or a clear history of rheumatic fever As controls, we used 600 cases in which there was no suggestion that the streptococcus could be incriminated these included 200 cases each of cancer tuberculosis and syphilis Of seventy-one cases of hypertension under 50 years of age a positive throat history was given in 60 per cent against 48 in the control group, tonsillectomy had been done in 35 per cent against 17 in the controls, rheumatic fever or valve disease had affected 14 per cent of the hypertensive group against 10 per cent in the controls These figures are not especially con

vincing except in the report of tonsillectomy here someone had considered the tonsils sufficiently at fault to require their removal in twice the proportion of cases as was true of the controls Actually, the per centage of tonsillectomies in the younger hyperten sive patients was about the same as that reported by 150 patients who had rheumatic fever or mitral stenosis or both In this rheumatic group from the records of the Johns Hopkins Hospital the tonsils had been removed in 36 per cent Presumably we all agree on the great importance of tonsillitis in touch ing off the series of events leading to rheumatic fever rheumatic carditis and allied conditions I do not know of any other disease in which the role of the tonsils is so significant and in which such role is so generally understood If a doctor does not advise tonsillectomy in such cases when would he? So we find this operation to have been done in 36 per cent Yet tonsillectomy had been performed in 35 per cent of our hypertensive patients under 50 years of age though I am quite sure from many discussions with colleagues that there is little bias among physicians against tonsils as an etiologic agent in hypertension So I think it is probably quite significant that ton sillectomy was considered advisable as frequently in the hypertensive group as in the rheumatic It seems to argue forcibly in favor of a close relation of demonstrably infected tonsils with premature hyper tension

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the mechanics of the circulation However, the same underlying renal pathology is found in these cases as occurs in other patients with hypertension the former authors showed that patients with mitral stenosis and hypertension that come to autopsy show granular kidneys cases of mitral stenosis without hypertension show smooth kidneys In other words these patients who have passed through undoubted rheumatic episodes show more than an even liability to develop arteriolar sclerosis and hypertension before middle life There is ample evidence in studies of pathologists for the conclusion that the rheumatic state known to affect the endocardium also damages arteries large and small The very high incidence of small vessel sclerosis and hypertension in patients with mitral disease is a further sign, I believe of the widespread effects of this infection

There are a number of questions for which we would like to find answers Why if infections are the basic cause of coronary disease do five men have this condition to every woman? We find this same sex difference in syphilitic cardiovascular disease yet the importance of the infection is not questioned I have often wondered whether the answer may not lie in the combination of infection and strain Men with inadequately treated syphilis are largely Negroes many of them laborers while women with syphilis lead somewhat more protected lives An analogous situation may exist in the background of coronary disease Congenital sex differences have been shown

showed very little difference from the control cases of cancer, tuberculosis, and syphilis Why the younger and older groups with hypertension differed in their experiences with the streptococcus involves so many possibilities that I shall pass the subject by without further remark It seems to me of some inter est that, whereas older patients with hypertension seem to conform with control cases this is not true of coronary occlusion as we have shown In the latter cases the report of excessive tonsillitis pervades all age groups though it is most striking among the younger patients

If repeated acute tonsilitis does affect the small and large arteries adversely it seems likely that pa tients so affected suffer episodes of streptococcosis or the rheumatic state, as we have discussed above Many of us have streptococcal infections and escape serious consequences perhaps these are the majority who have been reported as recovering without the systemic illness so similar to the rheumatic infection What is the effect of frank rheumatic infection on the small arteries? Several reports bear directly on this question

At least two studies are available Boas and Fine berg[8] found that 55 per cent of patients with mitral stenosis showed hypertension after the age of 40 Levine and Fulton[9] reported hypertension in 58 per cent of a large number of cases of mitral stenosis Attempts have been made to explain this association on physiologic grounds, i e, owing to alterations in

infection in systemic disease, including both hyper tension and coronary disease On a previous visit here Dr Danglade showed me the heart from a case reported by Dr Bohan—the case of a boy who died of coronary obstruction at the age of 14 He had suffered since birth from bouts of high fever due to recurrent pyelonephritis

Such then is our heresy If you believe it as sin cerely as your two honored guests you will probably fail your Board examination in cardiovascular dis ease All I ask is that you consider what I have said in your history taking and examination of patients time and your common sense will do the rest When you have become convinced you will be in position to do much to prevent the ravages of the greatest killer of our time

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in the anatomy of the coronary vessels Much work has been done on the relation of the blood lipids to arteriosclerosis Your Doctor Major has done very convincing work on the relation of guanidine to hypertension

How these factors fit into our picture, I cannot say I can simply report in this superficial manner, what I am told every day and what I see

So, I think the course of events must be some what as follows The streptococcus attacks the upper air passages, if the systemic invasion is of a certain type then frank rheumatic infection follows If this occurs, we can easily agree I think from the evi dence that coronary disease may result also a high liability to hypertension In this category of rheu matic infection I would include growing pains If, on the other hand the streptococcal infection fails to cause frank rheumatic manifestations yet a mild lingering illness that is probably the rheumatic state may be expected to ensue in a certain number of cases This milder form of rheumatic infection may occur regularly every year or two with each attack of tonsillitis This is not yet established in the mass medical mind but in my opinion there is no serious doubt that repeated tonsillitis is followed for some reason by a liability to coronary disease and prema ture hypertension

Our second most honored guest at least knows whereof I speak He went on record ten years ago to show his recognition of the importance of focal

infection in systemic disease including both hyper tension and coronary disease On a previous visit here Dr Danglade showed me the heart from a case reported by Dr Bohan—the case of a boy who died of coronary obstruction at the age of 14 He had suffered since birth from bouts of high fever due to recurrent pyelonephritis

Such then is our heresy If you believe it as sin cerely as your two honored guests you will probably fail your Board examination in cardiovascular dis ease All I ask is that you consider what I have said in your history taking and examination of patients time and your common sense will do the rest When you have become convinced you will be in position to do much to prevent the ravages of the greatest killer of our time

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IV

Urology and Internal Medicine

Herman L Kretschmer M D D Sc
1950



Herman Louis Kretschmer

Herman Louis Kretschmer was born in Chicago in 1879 He graduated from the School of Medicine at Northwestern University in 1904 Afterwards he practiced medicine in Chicago becoming also Clinical Professor of Surgery at Rush Medical College formerly part of the University of Chicago He has been president of the American Board of Urology the American Medical Association the Chicago Medical Society the American Urological Association and other medical societies He was also on the editorial board of the *Journal of Urology* and has made contributions in the field of genito urinary surgery He died in 1951

The many borderline problems in diagnosis that arise almost daily in the practice of the Internist and the Urologist are mute evidence of the close relation ship between Internal Medicine and Urology I wish to discuss with you some of these borderline problems which are encountered so frequently

The importance of a broad general training as a foundation for specialization again needs to be em phasized Having started my professional career as a general practitioner I speak from experience It is doubtful whether the large medical ward takes the place of a few years in general practice since the type of patient seen is entirely different Because of aware ness of this defect in our training there now is a tendency to have the trainee spend a certain amount of time with a well qualified general practitioner

The keystone in the arch of the practice of med icine is the patient himself The fact that a patient consults the urologist first does not necessarily make him a urological case Failure to recognize this fact often results in a long course of unnecessary treat ment

To elicit a good history takes time However one is often well repaid for his time and trouble Many of the preliminary facts may be obtained by an assistant but the final interpretation of symptoms and signs cannot be delegated to another

With the increasing mechanization of medical practice the history and physical examination are

frequently glossed over, and short cuts in the form of mechanical aids are used instead It is deplorable that *there are patients who have had innumerable tests* made, the reports of which they bring with them but of whom no physical examination was made! *The sad part of this routine is that it leads to useless* and unnecessary laboratory tests and adds to the already high cost of medical care

The So Called 'Male Climacterium'

The use of male climacterium is most unfortunate There is no justification for it In lieu of trying to determine the cause or causes of the patient s complaint it is used as a catch all and all too frequently the patient is given long courses of hormone injections *which obviously he does not need* and which are not the answer to his problem

Because of the age of the patient and his vague *and indefinite symptoms such as nervousness hot* flashes and insomnia a diagnosis of male climacterium is made The symptoms are frequently *psychic in origin The history is of the greatest im*portance and often gives the physician the clue to the cause of the patient s symptoms A little patience and a few direct questions on the part of the physician will generally ferret out the cause of these symptoms Simple direct questions will usually bring to light their origin, which may include such causes as family trouble or the fear of losing a job because of age or financial worries It is obvious that such patients will not benefit from hormone injections

Thyroid Disease and Urinary Symptoms

Urinary symptoms such as frequency urgency and burning occurring concomitantly with hyper thyroidism, are found frequently enough for the phy sician to bear this possibility in mind and hence to avoid a series of unnecessary bladder treatments

The presence of great nervousness a fine, fast tremor, and a rapid pulse make the diagnosis of hyperthyroidism perfectly obvious at the time of the first interview

I have recently seen several patients who had marked urinary symptoms due to hyperthyroidism and in whom the urological examination was nega tive In one case a few simple questions elicited the fact that the patient was taking three grains of thy roid a day without medical supervision

Parathyroid Disease and Urinary Disease

The specialist must never lose his medical point of view This statement is amply illustrated by the patient with recurring kidney stones The number of patients with parathyroid disease and kidney stones is not very large However the relationship between the two should be constantly borne in mind (1) especially when the patient has had one or more operations for renal or ureteral calculi (2) has passed calculi over a long period of time or (3) when, after a nephrectomy, now harbors stones in the remaining kidney

In a certain number of instances careful palpa tion of the neck demonstrates the presence of an

adenoma of the parathyroid gland When hyper plasia is present instead of an adenoma, palpable enlargement may be absent

The presence of bone cysts in a patient with kidney stones should at once arouse our suspicions of parathyroid disease The incidence of parathyroid disease in the average kidney stone case is very rare The diagnosis of parathyroid disease in the presence of renal and ureteral calculi is made from the changes in the blood calcium and blood phosphorus The incidence of kidney stones in parathyroid disease is fairly frequent [1]

Pernicious Anemia

Pernicious anemia with spinal cord changes resulting in bladder symptoms brings some patients to the urologist Frequency of urination difficulty and at times dribbling coupled with a few pus cells in the urine unfortunately result in local treatment in the form of irrigations and instillations without relief

The pallor unsteady gait the Romberg sign and changes in the knee jerks suffice to make a diagnosis of spinal cord bladder The blood count clinches the diagnosis

Spinal cord bladders due to pernicious anemia are not very common today because of the early diagnosis and treatment of pernicious anemia but the possibility must always be borne in mind [2]

Leukaemia

The urologist is frequently the first one to be consulted by the leukaemic patient The symptoms presented are hematuria and priapism

The hematuria is due to leukaemic infiltration of the kidney and the priapism due to leukaemic in filtration of the corpora cavernosum They are rarely both present at the same time

The patient with persistent priapism should at once call our attention to the possibility of leukae mia The onset is slow and the course progressive un til finally the priapism which at first was intermit tent is constant

There is nothing characteristic of the hematuria A tentative diagnosis can often be made from the history and the presence of an enlarged spleen or the enlarged lymph nodes The routine blood examina tion establishes the diagnosis except in rare instances when a sternal puncture must be made A complete urological examination is necesary to rule out other causes of hematuria

Backache

Backache in the minds of the laity means kidney disease and hence many patients with backache con sult the urologist Of the many kidney lesions re sponsible for backache I shall mention only a few hydronephrosis tumor stone tuberculosis poly cystic kidney solitary cyst and nephritis

If the urological examination is negative then

one is confronted with the consideration of all other causes of backache Among these may be mentioned arthritis of the spine, intercostal neuritis, fibrositis, prolapse of a disk and myositis

Probably the most common urological cause of backache in the young or middle aged male is chronic prostatitis [3] The prostate as the cause of backache is frequently overlooked because there are no symptoms directing attention to it Rectal examination showing changes in the prostate and the presence of pus in the prostatic strippings establish the diagnosis of chronic prostatis as the cause of backache after the previously mentioned causes have been excluded

Orthostatic Albuminuria

Because patients have been told that they have kidney trouble or for other reasons have requested urological consultation, it falls to the lot of the urologist to see patients with orthostatic albuminuria At times this presents a difficult diagnostic problem It is of great importance to know whether the patient has a nephritic or an orthostatic albuminuria

Young Haines and Prince have suggested that the following criteria be met before a diagnosis of orthostatic albuminuria is made (1) no past history of renal cardiovascular disease (2) no elevation of blood pressure (3) no white blood cells red blood cells or casts in the urine except intermittently and in small numbers (4) normal kidney function

(phthalein urea clearance dilution and concentration tests) (5) normal blood chemistry nonprotein nitrogen, blood urea total protein and albumin globulin ratio (6) negative plain x rays and normal intravenous urograms, (7) absence of albumin in urine secreted when the patient is in the horizontal position

Albuminuria of this type requires no treatment and there is no reason why the patient should not go about his activities in a normal manner

Association of Mental Disease and Urinary Disease

In some cases the presence of an unrecognized severe mental illness may be the cause of a difficult postoperative management It is because of this possibility that great care must be exercised in the problem of diagnosis and treatment of urinary tract disease in a patient who may have severe mental disease

I have in mind a young woman of 18 upon whom I operated for a large benign tumor of the bladder During her convalescence she was the most irascible patient in the hospital Nurses interns residents all thought she was a badly spoiled child Several years later she was admitted to another hospital with the diagnosis of dementia praecox from which she no doubt suffered at the time of the bladder operation and which explained her conduct during her post operative convalescence

Foci of Infection

Foci of infection in the teeth tonsils or sinuses may be responsible for lesions in the genito urinary

tract An acute attack of tonsillitis has resulted in an acute attack of pyelonephritis with or without gross hematuria

Chronic infection in the tonsils or teeth may re sult in chronic pyelonephritis An acute exacerba tion of a chronic tonsillitis has been followed by a profuse painless hematuria In a patient with profuse symptomless hematuria in whom the cystoscopic ex amination shows the presence of submucous hemor rhages we at once direct our attention to the teeth, tonsils and sinuses for the possibility of infection In some of these cases we have isolated the same type of streptococci from the urine as were isolated from the tonsil the teeth or sinuses thus establishing causal relationship

In some cases of chronic prostatitis the only etiological factor that can be demonstrated is the presence of infection in teeth, tonsils, or sinuses It may be difficult to establish the causal relationship between the distant foci of infection and the chronic prostatitis Even so it is the duty of the urologist to advise the patient to have these foci of infection eradicated purely as a health measure

The importance of eliminating foci of infection in the prevention of pyelitis of pregnancy was dem onstrated by Heaney and Kretschmer[4]

Since the elimination of foci of infection during pregnancy was established as a routine at the Presby terian Hospital the Hospital s incidence of pyelitis during pregnancy was reduced to 0 3 per cent, the

lowest incidence that I am familiar with The pa tients who were admitted with acute pyelitis all had failed to follow advice in the outpatient department to have their various foci cleared up

Rectal Lesions

The need for the urologist to evaluate gastro intestinal symptoms especially in the man of pros tatic age is important When the patient who has prostatic symptoms, presents himself for treatment and he gives a history of a sudden change in bowel habits our suspicion should at once be aroused for the presence of a carcinoma of the bowel or rectum, since changes in bowel habits are not due to prostatic obstruction

With the history of a change in bowel habits especial care must be used during the rectal examina tion to search with the examining finger for the presence of a carcinoma of the rectum If this is nega tive then proctoscopic examination and a barium enema are in order

I recently had two patients who presented them selves for operation for prostatic disease In giving their histories the patients mentioned that a change had taken place in bowel habits Rectal examination revealed that the patients had carcinoma of the rec tum in addition to their prostatic lesions

Recurring Attacks of So Called Cystitis in Women

I wish now to discuss an interesting group of women in whom a diagnosis of recurring attacks of

cystitis is made and in whom the urological examination is negative when the patients present themselves for examination They form a relatively large group and are seen both by the general practitioner and the urologist They travel from one doctor s office to another and receive all sorts of local treatments without results Many are treated with hormones vitamins, and ' shots of various kinds It is obvious that in dealing with this type of patient it is of the greatest importance to determine the cause of the recurring attacks of cystitis

In a very large number of these patients one has no difficulty in obtaining a history of disturbances in the intestinal tract It is striking how frequently these women give a history of chronic constipation loose and frequent bowel movements due to so-called spastic colitis or the use and abuse of cathartics

Some of these patients volunteer information that they have been under treatment for a spastic bowel without result I have been convinced for a long time that in many instances the trouble has a psychogenic origin

Indeed some cases of so-called cystitis are on a purely psychic basis This is usually established after the possibility of organic disease has been excluded Among the many psychological factors I have seen I would like to mention only a few recent or less recent suicide of the husband fear of pregnancy the marriage of a favorite son or daughter the fear of transmitting a long since cured venereal disease

Another frequently overlooked cause for the recurrent attacks of cystitis is amoebiasis The importance of an accurate history and diagnosis is illustrated by a recent patient who had many cystoscopic examinations ureteral dilatations intravenous and retrograde pyelograms and local bladder treatments for many years In addition she was taking a hormone a vitamin a barbiturate one of the sulfa compounds and potassium bromide

When I questioned her about her bowel movements she stated her bowels were fine, for she had five or six good movements a day Examination of the stool for amoebiasis pointed the way to proper treatment Examination of other members of her family revealed that they too had infestation with the amoeba

Some cases of frequency of urination are associated with dyspareunia At times it is difficult to obtain a history of dyspareunia because of modesty or disappointment

Then there is the occasional woman of the opposite type who has recurring attacks of so called cystitis and who tends to focus all her attention on her bladder symptoms boasting to interns residents and nurses of her sexual powers and of her many extra marital affairs I have seen women of this type who have had bladder treatment for many years What they need of course, is treatment by a psychiatrist

Stricture of the Ureter

Fortunately, the hyperenthusiasm for the treatment of so-called stricture of the ureter is on the wane All too frequently a diagnosis of stricture of the ureter is made, often on a purely symptomatic basis and without evidence of dilatation of the ureter or kidney pelvis As a result the patient is subjected to many ureteral dilatations without relief

Many of these patients who are women have definite psychological problems, such as a recent or impending divorce an errant husband, or in law troubles Naturally this group of patients will not be benefited by ureteral dilatations

On the other hand, in many of these women the symptoms are due to organic disease in the pelvic organs that need surgical correction For example, I recently saw a woman who had over forty ureteral dilatations without relief of her symptoms The underlying cause of her symptoms was an extensive endometriosis

It is evident that great care must be used in selecting cases for treatment by ureteral dilatation

Impotence

Most cases of impotence first consult the general practitioner

There is no problem of greater importance to the general practitioner internist or urologist than the problem of the patient with impotence Frequently a diagnosis of sexual neurasthenia is made

and the patient is given the brushoff This is most unfortunate An accurate diagnosis and the institution of proper treatment are imperative a cure may in many cases prevent the breaking up of a home since impotence is a common cause for divorce

There is no justification for prescribing hormones vitamins, shots etc, without a detailed examination of the patient The problem becomes a very simple one for the general practitioner if he will bear in mind the three common causes of impotence (1) general (2) local (3) psychic

1 *General Causes* The history and physical examination are the starting point to rule out systemic disease such as severe mental disease tabes dorsalis chronic nephritis diabetes intoxication due to alcohol or tobacco tuberculosis etc

2 *Local Causes* It is assumed that the external genitalia are normal The most frequent cause of impotence, in my experience is chronic prostatitis or seminal vesiculitis or both as they so frequently occur together The rectal examination and the microscopic examination of the expressed fluid serve to establish the diagnosis

3 *Psychic Causes* Next to chronic prostatitis psychic factors are the most frequent causes At times it may be difficult to elicit the psychic factor When the facts are presented to the patient namely that there is no organic cause for the impotence (no evidence of disease either systemic or in the genito urinary tract) and that there must be a psychic cause

for his impotence, it is generally quite easy to obtain his co-operation and to have him give the reason for his impotence

Impotence associated with severe mental disease is relatively rare but its possibility must always be borne in mind I recently saw a dentist whom I examined twice and each time he was negative, but he seemed highly nervous I then learned that he was under treatment by a psychiatrist, who told me that he was a serious mental case and might kill himself or maybe someone else

Elusive Ulcer

Because many of these patients consult the general practitioner first it is well for him to be on the alert for this type of bladder lesion

The history is that of frequent and often painful urination which has been present for a long time and gradually becomes worse and is not relieved by the various forms of treatment employed

Often the patient has had one or more surgical operations without relief and frequently the urine is clear and sparkling showing at most a few red or white blood cells

The patient with this history should have a cystoscopic examination which establishes the diagnosis at once

Congenital Anomalies of the Kidney and Ureter

Congenital anomalies of the kidney and ureter formerly were considered to be very rare With the

routine use of intravenous urograms by the urologist the general practitioner the internist and the surgeon many cases of renal anomalies are recognized Their proper evaluation is important

The mere fact that a patient has a bifid renal pelvis does not justify an operation If the patient complains of pain it must be remembered that the pain may be due to something else and that the congenital anomaly is hardly to be considered as a factor in the production of pain if the pyelogram is normal On the other hand in some of these cases of double renal pelvis double ureter a hydronephrosis may be present in one half of the double kidney and when present may be the cause of pain Failure to recognize this has resulted in appendectomy when a heminephrectomy was indicated In other words it should be remembered that the mere presence of a double kidney pelvis *and double ureter does not* justify operation

In an occasional case the ureter may have an anomalous insertion outside the bladder Cases in which the ureter is inserted in the floor of the urethra or in the vagina give a typical history of being wet day and night since birth and hence the diagnosis is perfectly obvious

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V

Surgery General and Otherwise

Claude F Dixon M D
1952

LITTLE did I think in my undergraduate days that I would be invited to speak to you members and former members of the faculty It would not have surprised me greatly however had one or all of you commanded that I stand before you in an attempt to defend myself scholastically

I accepted the honor of being your speaker on this occasion nevertheless most humbly to represent the multitude of doctors who have had the privilege of studying and working under Dr Bohan And I join in the consensus of those doctors when I say that we here pay tribute in a small way to one of the most outstanding internists of his time He bent the twig which was I in the direction in which he knew I ought to grow Having done this he transplanted me to the nursery of Dr Charles H Mayo who assiduously sprayed and cultivated until here I am heeled into the home soil for a few hours and that soil I find warm comforting and nutritive

You have seen or heard the title of these remarks In touching here and there on topics the title suggests I shall find myself in the paradoxical position for a speaker of listening—listening with the inner ear trying to hear what Pare Lister McDowell and the men who more recently taught me would say to surgeons who must meet the problems of today

These great figures of the long past and the recent past knew what was known of the science that underlay their craft and all of the art that was ex



Claude Frank Dixon

Claude Frank Dixon was born at Piedmont Kansas in *1893 He received his bachelor s degree from the University* of Kansas in 1919 and his M D degree in 1921 in 1926 the University of Minnesota granted him the M S degree in Surgery In 1926 he also began his teaching career at the University of Minnesota later becoming Professor of Sur gery as well as Head of the Department of Surgery at the Mayo Clinic where he has been a surgeon since 1928 spe cializing in general abdominal surgery and surgery of the thyroid gland He has contributed a large number of articles to medical journals

in touch with the world than we are I am thinking of the quack for whom I have no more regard than that held by a famous judge who justifiably disliked certain unpleasant persons Very likely you have heard his quatrain

> The queen of bees, though a social soul
> Is much averse to birth control
> And that is why one often sees
> So many many sons of bees

Sons of any letter of the alphabet we please, the charlatan has perfected the art of handling people In my opinion it is not necessary to possess great natural endowments in order to become a dependable surgeon However I do believe it necessary to have deep understanding of insatiable curiosity about and unlimited sympathy for human beings and their ailments Neither the science nor the art of surgery suffices

Technique

Yet technique cannot be too highly stressed in surgery Good painstaking techniques may make the difference between success and failure between life and death for the patient This is the view of master surgeons Dr C H Mayo once warned me

Never attempt a big operation through a small incision if you do sometime you will be obliged to make a longer and more adequate incision in an effort to correct your error

And it was Sir John Bland Sutton who said that if a surgeon desired to achieve great dexterity he

pressed in it We of today emulate them We are well based in science and we are given long training at the operating table Perhaps, without too much presumption, we can accept our seats in the guild, among those who have learned the trade

The Human Side of the Craft

But how do we do as fellow men? Our school and hospital work is arduous We gamble with our lives and with the fortunes of those who back us fully as much as did a man of fashion in the reign of Queen Anne—although our hazard is taken in a better cause Our gamble is not play It is a grim competition to hold our places as cadets in an officer candidates school where one demerit may mean dismissal with no hope of reinstatement As school boys and college youths we are not allowed to explore the humanities as medical students, interns and graduate students we shut ourselves away from the world, from recreation from social life from cultural reading Thus we learn of the life around us neither from books nor by contact Afterwards we think it a virtue that we kept our noses to the grindstone all those years

Virtue perhaps but wisdom? I don t know We know nothing but medicine we read nothing but medicine we think nothing but medicine and heaven help us we respect nothing but medicine We take not only the veil but the blinders

Some with whom nobody here would shake hands, and with reason, may in some respects be more

of all—one that was defined centuries ago, by the Father of Medicine Yet you I am sure are as alarmed as I am that in at least some medical schools all the students are being trained to be professors and none to be good sound general practitioners

Does it not seem strange that this should be so at a time when a concerted attempt is being made to interest the young doctor in general practice? Nor is the situation helped toward solution by those hospitals throughout the nation which deny their privileges to all men regardless of ability or character unless they are certified by at least one of the many specialty boards At present a new board seems to come into existence every two or three years

Very likely it is absurd to question whether still another board will be formed in the field of the sincere gentleman with whom I recently conversed He informed me that he was specializing in surgical work. When I asked in what field he replied Inguinal hernia

Not realizing that he was serious I immediately got in deeper by telling him of a young man who had specialized in eye, ear nose and throat work and who after a few years informed a general practitioner that his field was too large and that he was confining himself to diseases of the nose Thereupon the general practitioner inquired Which nostril?

That anecdote reminds me of another which recently I heard in the course of a most learned address delivered by that great citizen whose name

should first observe a woman crocheting or sewing a hem and then should try to do it Again, recently Sir Heneage Ogilvie in a paper entitled The First Inch of the Duodenum ' stressed the importance of dexterity lest injury to the duodenum or common bile duct be done in the course of cholecystectomy

Hath not the potter power over the clay ? asked the Apostle Paul So must the good surgeon have command of the much more precious medium wherein he works

Specialization

The mechanical part of surgery, however, is by no means coextensive with the complete art of the surgeon Although he relies to a great extent upon his friends the internists to a degree he also must be a diagnostician and as time passes I wonder if all physicians including those of us who are in the field of surgery, are becoming too highly specialized Does the surgeon depend more than he should on the diagnostic acumen of the internist? If the surgeon accepts the patient for operation, it will be the surgeon who will be accountable under the law and to *his own conscience for the patient s life and well* being Should the surgeon accept the patient? It will be nothing derogatory to the internist if the surgeon asks this question He must ask it he must make his own diagnosis The existence of specialization does not relieve him of responsibility

Those of you who are teachers in the medical school are engaged in the most honorable specialty

the whip, so it can be ruined by politicians from without

I believe that medicine and surgery can progress only if they are allowed to remain in the hands of honest well balanced scientists and doctors The autocratic direction of men and women who are unfamiliar with the problems of the physician and surgeon and who perhaps are unsympathetic towards them would be to put it mildly stultifying

To be sure no institution is perfect and unfavorable criticism particularly if it is sound and kind is the best gift that an organization or a man can receive Much recent unfavorable criticism of medicine and medical men however, has been misdirected as a result of pure ignorance possibly mixed sometimes with malice In his presidential address to the American Physiological Society Dr Maurice B Visscher mentioned an outstanding scientist whose experimental work required that he use alcohol He also had a small still in his laboratory What laboratory man has not? Usually it supplies distilled water But the juxtaposition of a still and a supply of alcohol could have only one significance to a certain uninstructed politician who reported the scientist to police authority and the scientist was arrested At the hearing the judge asked Is it true doctor that you own and operate a still?

Yes replied the scientist

After a severe sentence had been announced the convicted man said Your honor I should like also to plead guilty to rape

Bernard Baruch, has become synonymous in the minds of Americans with the title elder statesman He asked, Are surgeons and medical men becoming too highly specialized?

Then he answered his own question in the fol lowing way A man entered a bird store, he said and bought some canaries As the purchaser was leaving the shop he asked the proprietor what kind of food the canaries should have The proprietor s instruc tions were to place a handful of worms in the bird cage The male canaries would eat the male worms he said, whereas the female birds would eat the fe male worms

But, asked the purchaser how can I tell whether I am giving them male or female worms?

Oh that! replied the shop owner You must find that out at the worm store here we deal only in birds

You see what I am getting at without my labor ing the point In my estimation a general surgeon should be able to give expert attention to any surgical condition that arises in the abdomen and according to my notion this declaration does not exclude gyne cologic disorders Certainly a patient with gallstone colic uterine prolapse and hemorrhoids does not need the service of three surgeons

Outside Interference

Just as medicine and surgery can be smothered by those within the medical field who would crack

done while one is young the slowing of thought and narrowing of imagination which are said to characterize the process of aging will serve as barriers to accomplishment This statement is true only if and when the surgeon accepts it as true and retreats into more or less routine clinical practice

Take the case of penicillin one of the weapons against infection referred to a moment ago By one of the triple plays that add to the pleasure of working in Rochester (this play was Eckman to Hewitt to me) I learned that Gordon Home in his volume *Roman London*, related that excavations in London uncovered a stone seal dating from the time of the Roman occupation Apparently it was used by a physician or apothecary to stamp his ointments and it read freely translated

Caius Silvius Tetrich s swab-on ointment for an attack of rheum in the eyes

The startling thing about it was the partial word penicill which if completed probably would have read penicillium This means brush sponge, or lint So the old Roman did not dispense a penicillium ointment as first glance at the inscription suggests and that spoils the story Rudyard Kipling however more than half a century ago stated in effect that the forefathers of us of the present day brought about the rapid healing of wounds by applying mold from certain plants All that is enlightening but the point is that we self-congratulatory wonder boys of contemporary medicine remained igno-

'So' asked the judge 'you have committed rape, too?

'No, I have not, replied the doctor but since I happen to possess all the natural attributes with which to accomplish it, I am apparently guilty"

Research and the Need of Clinical Trial

No medicine surgery, or research cannot be successfully put under the control of those who know nothing much about them The problems are complex partly because this is an era of frequent and formidable discoveries Various agents made available in recent years have helped to reduce the incidence of infection following surgical operations Against each infectious process there seems to be a new weapon It has been stated recently that some preparations now available are so new that new diseases must be discovered to furnish a field for their application Notwithstanding the wonders wrought by these agents not one of them is intended to take the place of aseptic surgery skilfully performed

So the clinical surgeon stands in close relationship to research, but his exact role seems different to different commentators Certainly results of research in surgical fields must be carefully studied before they are applied to patients Most clinical surgeons do not find time or fail to take time to conduct research Perhaps current opinion discourages the mature surgeon from participation in research, for in some quarters it is the consensus that unless research is

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rant of all this lore until an elderly physician, now a knight, Sir Alexander Fleming observed that a mold which contaminated his culture media caused lysis of colonies of staphylococci This mold he identified as penicillium Do we need more acute observation in the laboratory? Or would a more encyclopedic per spective of our craft, as Charles G Osgood might call it keep us abreast of the old timers?

The story of penicillin reminds me that nearly a century ago English physicians recorded the rapid healing of wounds after application of a poultice of cow manure So far as I know this is one substance which is yet to be sponsored by a nation wide radio network I cannot vouch for its therapeutic value but in recent research it has been found to be rich in chlorophyll and vitamin B12 also it most likely contains one or more of the steroids

It seems to me that I have wandered a good deal in this talk and have not said very much on any one thing But I learned the method from one of my revered surgical chiefs When he descended from his pedestal and took his seat on a cracker barrel, people remembered what he said I never having ascended from the cracker barrel find his example relatively easy to follow I can only hope for comparable re sults

VI

A Quarter Century of Medical Experience

Paul D White M D
1953

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TWENTY FIVE years are but a tiny fraction of time in the life of the planet on which we live, but for most of us mortals they comprise about half of our working careers and less than seven such periods of time have elapsed since George Washington became our first President * Most interesting and impressive of all for physicians is the fact that this last quarter of a century has seen more advances in medical science than had been accomplished in all the ages before Some of us older physicians have witnessed this extraordinary metamorphosis and are asked now and again about it Although such reminiscence is often interesting and picturesque its chief value is in helping to plan for the present and for the future I myself hope to live long enough to be of some use in the progress of medicine to come having had a background of a growing experience during the last few decades Happily now, however I am but one of many thousands who have the same goal of adding to our medical knowledge whereas a generation ago there were only a relatively few hundred in this country who had the good fortune the time the health, and the stimulating tradition around us to explore

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*Dr White Clinical Professor of Medicine at Harvard Medical School presented this address at the convocation September 25 1953 commemorating the twenty fifth anniversary of the School of Medicine of the University of Southern California at which he received the honorary degree of Doctor of Science and in Kansas City on September 27 1953 in honor of Dr Peter T Bohan on the Bohan Lectureship



PAUL DUDLEY WHITE

Paul Dudley White was born in Roxbury Massachusetts in 1886 He attended Roxbury Latin School and Harvard University which granted him the A B degree in 1908 and the M D degree in 1911 He also studied in London in 1913 14 and in Vienna in 1928 29 Since 1914 he has taught in the Harvard School of Medicine His research teaching and practice have been chiefly in the field of heart disease He has been president of the American Heart Association and has participated in many medical missions in foreign countries Besides articles in various journals he has written *Heart Disease,* 1931 fourth edition 1951 *Heart Disease in General Practice,* 1937 *Electrocardiography in Practice* (with Ashton Graybiel) 1941 second edition 1946

given almost exactly fifty years ago to the medical students on the occasion of the opening of the medical faculty of the University of Toronto on October 1, 1903 Osler was Professor of Medicine at Johns Hopkins University at that time

> It seems a bounden duty on such an occasion to be honest and frank so I propose to tell you the secret of life as I have seen the game played and as I have tried to play it myself You remember in one of the Jungle Stories that when Mowgli wished to be avenged on the villagers he could only get the help of Hathi and his sons by sending them the master word This I propose to give you in the hope yes in the full assurance that some of you at least will lay hold upon it to your profit Though a little one the master word looms large in meaning It is the open sesame to every portal, the great equalizer in the world the true philosopher s stone which transmutes all the base metal of humanity into gold The stupid man among you it will make bright the bright man brilliant and the brilliant student steady With the magic word in your heart all things are possible and without it all study is vanity and vexation The miracles of life are with it the blind see by touch the deaf hear with eyes the dumb speak with fingers To the youth it brings hope to the middle aged confidence to the aged repose True balm of hurt minds in its presence the heart of the sorrowful is lightened and consoled

a bit into the unknown The prospect is bright for the future Those of us who began our careers at the dawn of what seems to have been the golden age of medicine talk of our good fortune in having been born when we were but I daresay that those of you who are beginning or who have recently begun your careers today *will be justified in boasting of your own* still better fortune a quarter of a century hence

It will be I am sure, more interesting and profitable for you who are listening to me if I speak more of my own personal experiences than if I should give you a review either of medical advances in general or of the history of your own school in particular, about both of which you will hear much more factually from others Lest I be thought either egotistical or egoistical with respect to my own special field of interest I would hasten to say at the start that my entrance into it was more or less accidental and my pursuit of it though exciting routine I am sure that I could have been equally happy in other special fields, including general practice that are now open to the medical student and to the young physician I hope nevertheless that my own limited experience may be of some interest to you

Those of us who have been fortunate enough to have survived a good many years of a medical career are asked what we believe to have been factors behind any success that we may have achieved So far as I am concerned I *believe that I cannot do better than to* read you two quotations from an address by Osler

that work consists of whatever a body is obliged to do and that play consists of whatever a body is not obliged to do *

And now the second quotation—

How can you take the greatest possible advantage of your capacities with the least possible strain? By cultivating system I say cultivating advisedly, since some of you will find the acquisition of systematic habits very hard There are minds congenitally systematic others have a lifelong fight against an inherited tendency to diffuseness and carelessness in work A few brilliant fellows try to dispense with it altogether but they are a burden to their brethren and a sore trial to their intimates I have heard it remarked that order is the badge of an ordinary mind So it may be but as practitioners of medicine we have to be thankful to get into this useful class Let me entreat those of you who are here for the first time to lay to heart what I say on this matter Forget all else but take away this counsel of a man who has had to fight a hard battle and not always a successful one for the little order he has had in his life—take away with you a profound conviction of the value of system in your work

I have had the good fortune to have lived at a time when it was possible to work more diffusely in

* When I read this passage to my wife the other day she observed that there is another master word in medicine at least equally important and to this I agree That other master word is LOVE that is love of humanity

It is directly responsible for all advances in medicine during the past twenty five centuries Laying hold upon it Hippocrates made observation and science the warp and woof of our art Galen so read its meaning that fifteen centuries stopped thinking and slept until awakened by the *De Fabrica* of Vesalius which is the very incarnation of the master word With its inspiration Harvey gave an impulse to a larger circulation than he wot of an impulse which we feel today Hunter sounded all its heights and depths and stands out in our history as one of the great exemplars of its virtues With it Virchow smote the rock and the waters of progress gushed out while in the hands of Pasteur it proved a very talisman to open to us a new heaven in medicine and a new earth in surgery Not only has it been the touchstone of progress, but it is the measure of success in everyday life *Not a man before you but is beholden to it* for his position here while he who addresses you has that honor directly in consequence of having had it graven on his heart when he was as you are *today* And the master word is WORK a little one, as I have said, but fraught with momentous sequences if you can but write it on the tables of your heart, and bind it upon your foreheads But there is a serious difficulty in getting you to understand the paramount importance of the work habit as part of your organization You are not far from the Tom Sawyer stage with its philosophy

'that work consists of whatever a body is obliged to do and that play consists of whatever a body is not obliged to do *

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medicine than can be done today to have had a hand in three thrilling medical careers—the practice of medicine the teaching of medicine, and clinical research The first I have enjoyed most, I suppose because of the close human relationships that are the privilege of a practicing physician My father before me acquired a host of friends among the families he took care of as a general practitioner With that example and an appreciation of that wonderful experience of his while I was still a boy, I recognized very early what happiness could come from such friendships I suppose that that has colored my career through all the years I have enjoyed these relationships and have learned slowly but surely that the successful practice of medicine depends not so much on the instrumental techniques for diagnosis or on the drugs or other therapeutic measures that we use as on the co operation and devotion of our patients to be secured by establishing the best possible ties with them on the very first occasion that they seek our advice This human relationship has been a great asset of the medical profession since the days of Hippocrates or even before that but at first it was based on very fragile grounds

Much of the medicine that was practiced over many centuries in fact right down to the end of the first World War was what we now call psychosomatic The little that was known had to be applied *in fullest degree in order* to accomplish anything and for such application it was always necessary for

the physician to secure the complete co-operation of the patient I am sure that very much help was given by my father through his sugar pills in the application of ordinary common sense measures though there was little or nothing that was then specific in therapy Nowadays with so many specific cures of so many diseased conditions we are I fear likely to be a bit careless of our opportunity to apply this experience of the past It is thrilling now to be able to add to our spiritual comfort of patients which was almost all that was available in the old days the specific curative or helpful somatic therapy of today Not only can we prolong many lives today we can make those longer lives more comfortable and useful It is hard to realize for example what a change has come in our attitude about subacute bacterial endocarditis Only ten years ago and for the twenty years before that I dreaded to make the diagnosis inasmuch as the mortality was close to 99 per cent and death came slowly Now with the possibility of cure in 80 per cent of the cases one eagerly makes the diagnosis as early as possible And more important still one can give advice that can in many cases probably prevent the disease itself Those of us who are practicing medicine should realize the far happier lot that is ours today not only in being able to do more for our patients who become our friends but also in keeping such friends alive and often comfortable for many years longer than would have been possible a few decades ago That enriches our lives One other good

fortune that is ours in this country today is that with our richer opportunities to make advances in medical science we can play a role in world medicine and bring help to those patients of ours who come from abroad In this way we can establish friendships with citizens of other countries who may be playing an im portant role in contemporary world history Such an experience is a good antidote for the extreme na tionalism that sometimes threatens us and for the chauvinism with its parochialism and provincialism that are such common sins of mankind Sir Thomas Browne in the *Religio Medici* wrote National re pugnances do not touch me nor do I behold with prejudice the French Italian, Spaniard or Dutch, but where I find their actions in balance with my countrymen s I honor, love and embrace them in the same degree The more I myself see of the fine people from other lands who have become patients of mine the more I agree with those observations that I have just quoted

And now a word about teaching The teacher of medicine like the teacher of any subject can be thankful for his privileges in keeping a contact with the young The stimulus which comes from teaching never ends and is perhaps the most important means of maintaining a close touch with medical progress This relationship applies not only to young students but also to those of any age whom we may be fortu nate enough to have in our classes or clinics Grad uate teaching I have found as stimulating as under

graduate teaching and, of course in a special field such as mine one has a preponderant teaching experience with this group Two phases of this experience come to my mind The first is that in the teaching of clinical medicine a close contact with private patients is invaluable Happily now, in view of the change in the customs of hospitals throughout the country even the full time professors of medicine have a share in the care of private patients Once upon a time the professor of medicine had only a very casual contact with the individuals in the hospital wards under his charge He did not get to know them as friends although in former days he did have his *private practice* too to keep his feet on the ground by maintaining human relationships with sick people The part time teacher of medicine has never had any difficulty in this respect but for a while the usefulness of the full time clinical professor was somewhat hampered The situation now has in part at least improved Also happily there is a less impersonal relationship today between the professor and his students as well as between the professor and his ward patients because of the subdivision of medical classes into smaller and smaller sections and groups for more intimate teaching In this country happily there has always been a better situation in this respect than in some countries where there has been too great a gulf between the Herr Professor and his students and ward patients One must be constantly on

fortune that is ours in this country today is that with our richer opportunities to make advances in medical science we can play a role in world medicine and bring help to those patients of ours who come from abroad *In this way we can establish friendships with* citizens of other countries who may be playing an important role in contemporary world history Such an experience is a good antidote for the extreme nationalism that sometimes threatens us and for the chauvinism with its parochialism and provincialism that are such common sins of mankind Sir Thomas Browne in the *Religio Medici* wrote, National repugnances do not touch me nor do I behold with prejudice the French Italian Spaniard, or Dutch, but where I find their actions in balance with my *countrymen's I honor, love and embrace them in* the same degree ' The more I myself see of the fine people from other lands who have become patients of *mine the more I agree with those observations that I* have just quoted

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wants to accomplish much of anything in that field in view of the complicated programs of today Simple clinical observations and investigations are however still possible Everything has not yet been learned or explored in the simple study of patients

To those who wish to do more than medical re search or who wish to add medical research to a pro gram of practice and teaching very careful planning is necessary Here the second important advice of Sir William Osler is in order that is the establishment of a careful system in one s planning and work Hours must be set religiously aside for reflection, ob servation and investigation and for writing Mid night oil may need to be burned and can be I be lieve from my own experience without hazard to life or health if one maintains a proper balance of rest periods and also a healthy program of exercise Finally in one s plans for research I have found that association with colleagues younger older or of contemporary age is of the greatest importance To work wholly alone is not only too arduous but it is likely to be wasteful One needs the control advice and help of fellow workers and of many hands One of the pleasant experiences of the last decade or two in research just as in teaching and in practice has been the opportunity to become acquainted, and to work with young physicians from other countries I myself had originally a rich experience of a year in London at the very beginning of work in my special field Now such experiences abroad are not so neces

watch to avoid this danger of the impersonal practice of medicine

The second educational experience that I would mention is that of the utilization of private patients for one's teaching I have found that my greatest value in teaching of clinical medicine has developed through the use for this purpose of my private patients, the great majority of whom are very co-operative in fact enthusiastic about their utilization in this way Nowadays with higher standards of living and with the improvement in meeting the costs of illness more and more individuals have acquired the status of private or semi private patients No longer do we see so many wards full of derelicts or very poor people who can be considered impersonally as subjects for the medical school

The third field in which I have had the good fortune to play a small role is that of clinical research Although it is still possible to combine, to some degree at least private practice teaching and research, it has become more than a full time job for anyone to accomplish much in any of these fields if he tries to do them all Each field really requires a minimum of an eight hour day and when the three are added together they consume more than the twenty four hours available Here of course, the master word work has been essential in the past and it is still more essential now Probably we must become resigned to the realization that it is necessary today to spend the major part of one s time in medical research if one

that time of course little or nothing was known about disease, but much more attention was paid to the maintenance of good health We need to get back more to that point of view, certainly in the medical teaching of today Occasionally in the centuries that have followed there has risen an inspiring prophet of better things to come Such a man was Oliver Wendell Holmes who in 1860, at the meeting of the National Sanitary Association wrote

What makes the Healing Art divine?
  The bitter drug we buy and sell,
The brands that scorch the blades that shine,
  The scars we leave, the cures we tell?

Are these thy glories holiest Art —
  The trophies that adorn thee best —
Or but thy triumph s meanest part —
  Where mortal weakness stands confessed?

* * *

Though on the field that Death has won
  She save some stragglers in retreat —
These single acts of mercy done
  Are but confessions of defeat

What though our tempered poisons save
  Some wrecks of life from aches and ails
Those grand specifics Nature gave
  Were never poised by weights or scales

* * *

sary as they were before this country developed its medical leadership, and the reverse has become true However, we can still learn a great deal from our colleagues from foreign lands both by enlisting them in our researches at home and by taking part ourselves in studies being carried on abroad where conditions of life and health may be different from those *in the U S A*

Before concluding this address I would speak briefly of my interest in public health Sometimes at the beginning of one s medical career one becomes so absorbed in the demands of the diagnosis and treatment of sick patients that one loses sight of the predominant importance of preventive medicine As the years go by, however, experience turns one s attention more and more to this field, and happily in the medical schools of today there is beginning to be much more attention paid to the study and the prevention of the causes of disease than was true when I was a medical student We often regarded the teaching of preventive medicine that we received as the least interesting and least important of all our medical courses It was sometimes presented to us in a way that made it seem as dry as dust That unfortunate situation is changing and we are going back somewhat to the interests of our remote medical ancestors who nearly a thousand years ago established rules of health, as in the *Regimen* presented in manuscript and as one of the first printed books by the University of Salerno the site of the first medical school At

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* * *

In vain our pitying tears are shed
  In vain we rear the sheltering pile
Where Art weeds out from bed to bed
  The plagues we planted by the mile!

* * *

And lo! the starry folds reveal
  The blazoned truth we hold so dear
To guard is better than to heal —
  The shield is nobler than the spear!

And now as we look forward to the future let us try to deserve that wonderful tribute paid to physicians by Robert Louis Stevenson— There are men and classes of men that stand above the common herd the soldier the sailor and the shepherd not infrequently, the physician almost as a rule, he is the flower such as it is of our civilization

VII

Prognosis in Coronary Artery Disease

Roy W Scott, M D

1954



ROY WESLEY SCOTT

Roy Wesley Scott was born in New Albany Indiana, in 1888 He graduated from Indiana University in 1910 and obtained his M D degree at Western Reserve University in 1913 later doing graduate work there and at the University of Vienna In 1915 he joined the faculty of Western Reserve University becoming Professor of Clinical Medicine in 1929 He has been president of the American Heart Association and of the Central Society for Clinical Research

THERE is no aspect of the subject coronary artery disease more difficult or fraught with more uncer tainty than that of prognosis The validity of this statement is perhaps more apparent to those in life insurance medicine than to the practicing physician, as they deal annually with thousands of cases of *coronary disease many of whom in the prime of life* have died suddenly and unexpectedly with no pre vious symptoms of coronary insufficiency Often a man is accepted in the forties as a standard risk for a sizable policy only to drop dead of coronary occlu sion after paying a few years premiums On the other hand, there are individuals with clear cut symptoms of coronary insufficiency and the anginal syndrome who with care may survive a goodly number of years Furthermore it is not uncommon to find at post mortem widespread coronary arteriosclerosis that was clinically silent To explain these apparent vagaries we must examine some of the more recent work dealing with the anatomy, pathology and phy siology of the coronary bed Although this work does not solve all the problems it does throw considerable light on the question Why is the prognosis in cor onary disease so difficult to determine?

The Anatomic Pattern of the Coronary Arteries

Observations on the blood supply to the heart based on careful anatomic dissection date from the middle of the sixteenth century Since that time sev

eral methods have been devised to visualize not only the larger arteries but also the smaller ramifications of the coronary bed

In 1921 Gross published a method of visualizing the coronary bed by injecting barium sulphate and gelatin and then taking stereoscopic roentgenograms of the injected specimen Although yielding more information than any previous techniques, Gross method was open to criticism because his roentgenograms had to be interpreted stereoscopically and since the blood vessels from the various planes of the heart overlap, the interpretation of such films is very difficult To overcome the major objections to Gross method Schlesinger in 1938 devised a unique method of dissecting the heart, so that the injected coronary circulation could be visualized in one plane We have recently modified his method of dissection so as to preserve the architecture of the aortic and pulmonary valves and have substituted for his lead phospate agar a suspension of barium sulphate in an aqueous ammoniated solution of liquid latex

In the routine study of human hearts by Schlesinger s technique it now has become apparent that the anatomic pattern of the coronary arteries is such that one may divide human hearts into three patterns 1) Those in which the right coronary artery supplies all the right ventricle a part of the septum and part of the left ventricle (see Fig 1) Such a heart we may call a right coronary artery preponderant 2) Those in which the right coronary artery

supplies only the right ventricle and the posterior part of the septum and the left coronary artery supplies the left ventricle and the anterior part of the septum (see Fig 2) Such a heart we may designate as one with a balanced circulation 3) Those in which the left coronary artery supplies all the left ventricle all the septum and a part of the right ventricle (see Fig 3) Such a heart we may designate as left coronary artery preponderant

Schlesinger has found and in a smaller series of cases we have been able to confirm, that the clinical course of a patient with coronary arteriosclerosis is definitely affected by the congenital pattern of his coronary circulation For example hearts with left atrial preponderance are the most vulnerable to coronary disease showing the highest incidence of coronary occlusion with myocardial infarction usually resulting in death The pattern of the coronary tree is such that little collateral circulation from the right coronary artery is possible The heart best equipped to adjust itself to coronary disease is the one with a balanced circulation where the collateral anastomosis between the terminal arterioles of the two main vessels is easily established In this group are the majority of hearts that survive one or more infarctions Somewhat intermediate in vulnerability to coronary disease is the heart with a right coronary preponderance About 50 per cent of human hearts both male and female show the right coronary artery preponderance when the arterial bed is visualized at

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confirmed They concluded that the adequate stimulus for the development of intercoronary anastomosis was arteriosclerotic narrowing or occlusion of the coronary arteries As this process leads to myocardial ischemia the thought occurred to us that perhaps ischemia alone without coronary diseases might be the important factor in the development of precapillary coronary anastomosis Observations on two cases confirmed this suspicion

Case 1 A female aged 52 was admitted to the hospital moribund and died within four hours Red blood cells numbered 700 000 and the blood smear had the typical appearance of pernicious anemia The post mortem findings supported the diagnosis Visualization of the coronary bed revealed very extensive intercoronary anastomosis with no evidence of coronary disease

Case 2 A female aged 52 had a history of aplastic anemia for several years The red blood cells varied between 1 5 and 2 5 million over the three year period that the patient was under observation Visualization of the coronary bed revealed extensive intercoronary anastomosis and no coronary arteriosclerosis

The findings in these two cases of profound anemia are interesting in the light of the clinical observations of Amadeo published in 1944 As a practitioner in a rural district of Puerto Rico he became impressed with the fact that his patients over 45 with chronic anemia due to uncinaria infestation

post mortem In hearts showing a balanced circulation the type best equipped to adjust to coronary disease women predominate whereas the anatomic pattern most vulnerable to coronary disease, namely, left preponderant, is found more often in men than in women Thus we see that in the presence of coronary disease the capacity of a given heart to carry on is greatly influenced by its coronary pattern and until it is possible to determine the pattern in the living patient one important factor in prognosis must remain unknown

Although the anatomic pattern of the coronary circulation plays an important role in the development of intercoronary collateral anastomosis there are other factors to be considered The question as to whether or not the coronary arteries were end arteries was debated among anatomists and physiologists for many years but the consensus now is that the anastomotic circulation does exist within the heart However the functional significance and circumstances which affect the development of such a circulation are not entirely settled

Gross Spalteholz and others believed as a result of their studies, that an anastomotic circulation developed between precapillary vessels as the result of age This conclusion was not verified by Blumgart and his associates who found no significant anastomotic connection between the right and left coronary arteries in even senile patients who had little or no coronary arteriosclerosis These observations we have

confirmed They concluded that the adequate stimu lus for the development of intercoronary anastomosis was arteriosclerotic narrowing or occlusion of the coronary arteries As this process leads to myocardial ischemia the thought occurred to us that perhaps ischemia alone without coronary diseases might be the important factor in the development of precapil lary coronary anastomosis Observations on two cases confirmed this suspicion

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and inadequate diets rarely had angina or coronary occlusion and in spite of their anemia were able to do strenuous physical exercise with extreme ease He postulated solely on the basis of his clinical experience that the existence of *a moderately severe but* tolerable anemia for a sufficient length of time is capable of exerting a beneficial effect on the normal human heart If chronic myocardial ischemia is a factor in developing intercoronary anastomosis as it appeared to be in our two cases it may well explain Amadeo s observations

In this connection it would be interesting to know the incidence of myocardial infarction in people with chronic anemia and also in individuals living at high altitudes such as Peru

Another factor which influences the development of intercoronary anastomosis, and hence prognosis is the rate at which coronary narrowing occurs Proceeding slowly the heart is given ample time to open collateral channels and compensate for the resulting ischemia So extensive may be the collateral circulation in some hearts usually in the older age groups, that in spite of widespread coronary arteriosclerosis the patient during life had no symptoms of coronary insufficiency and indeed may have sustained occlusion of a major vessel without infarction of the myocardium

I have a 79 year-old male patient whom I have *examined at least annually for the past ten years* Judged by his capacity to exercise without anginal



Fig 1 The *coronary bed* of an 18 year old male In this and other illustrations the heart was opened by the Schlesinger method so *that it lies on one place* and *the coronary bed* was visualized by the injection of a suspension of barium sulphate in an aqueous *ammoniated solution* of liquid latex The interventricular septum is removed and its site is marked by the letter O so that the right ventricle lies to the right and the left ventricle to the left of the letter O Note that in this heart the right coronary artery supplies all the right ventricle the septum and a considerable part of the left ventricle hence it is an example of right coronary artery preponderance



Fig. Th ronary bed in a year old male showing a balanced circulation and normal coronary arteries

symptoms and by the fact that he exhibits less S T depression in the electrocardiogram with a given amount of effort with the two step test of Master he now has a more adequate coronary circulation than he had ten years ago Very likely he was fortunate enough to have been born with a balanced circulation and the sclerotic process in his coronary bed had advanced at a slow rate From our observations and those of Blumgart and Schlesinger it appears that the rate at which collateral circulation can develop is slow Sudden occlusion of a main coronary artery from thrombosis with relatively little generalized coronary arteriosclerosis is often fatal and a massive infarction is found at post mortem

Handicapped as we are in predicting whether or not any given individual will develop coronary artery disease it should be emphasized that with the knowledge accumulated from clinical and pathological observations over the past thirty years we may now estimate more accurately than formerly the incidence of coronary artery disease as it may occur in a large group of people This obviously is important from an actuarial standpoint For example it is well established that persons with arterial hypertension exhibit a significantly higher incidence of coronary arteriosclerosis than do people with normal blood pressure The incidence of coronary disease in normotensive non diabetic women under 50 is notoriously low as compared to men of the same age

As I have indicated above, the most important feature relating to prognosis cannot be determined in the living patient Nevertheless, it cannot be said that no progress whatever has been made in predicting at least in individual cases which will do well and which will not particularly patients with coronary occlusion and myocardial infarction Here we may consider the immediate prognosis and the remote or ultimate outcome

Immediate Prognosis

Early studies placed the immediate mortality of coronary occlusion as high as 50 per cent More recent observations have shown it to be much lower and depending to some extent on the economic status of the patient the figures vary between 20 and 30 per cent Andrus found that in a series of 888 cases of coronary occlusion at the Johns Hopkins Hospital the mortality rate among private patients was 18 per cent as compared with nearly 30 per cent among ward patients who received the same treatment He thinks that earlier diagnosis and hospitalization account for the difference

Of great prognostic import is the persistence over several hours of peripheral circulatory collapse with cyanosis sweating and systolic blood pressure under 80 mm of mercury The mortality in such cases is upward of 90 per cent As fever and leucocytosis vary with the amount of myocardial necrosis it is not surprising that Levine found that the mortality was

71 per cent in patients with temperatures above 103 F as compared with 29 per cent in those with fever below 103 F Where the white count was under 15,000 the mortality rate was 16 per cent and over 15 000 it was 54 per cent Dyspnea and the presence of left heart failure with rales at the lung bases raise the mortality above 50 per cent A persistent tachy cardia (120 or above) and the appearance of ventric ular tachycardia are grave prognostic signs Compli cations such as pulmonary infarction and periph eral vascular occlusions affect the prognosis ad versely Even in patients who develop none of the above signs known to raise the mortality in coronary occlusion there is no sure method of predicting their outcome certainly for the first two weeks Following this period and provided no complications have ap peared one can then with increasing confidence pre dict their recovery

Ultimate Prognosis

From the published data it appears that between 65 and 70 per cent of patients outlive their first attack of coronary occlusion that about 25 per cent survive more than ten years and about 50 per cent for five years or longer The average survival time in 101 cases followed by Levine was 41 1 months All ob servers agree that the most important single factor influencing the ultimate prognosis is the age of the patient at the time of the initial attack

Younger patients live longer and their recovery is more complete Finally it should be emphasized that

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the ultimate outcome in a patient with coronary occlusion is influenced by the care given immedi ately following the acute episode Such work as has been done indicates that an important element in the development of collateral channels in the coron ary beds is the element of time, and the process is a slow one This has been emphasized recently by Blumgart and his associates as a result of animal ex periments and affords, I believe sound reason for re ducing the patient's physical and emotional outlay for many weeks following an attack of coronary occlu sion with myocardial infarction Early ambulation of such cases as has been recommended in some quar ters recently certainly cannot be justified

In summary, I may say that as a result of post mortem studies of the coronary circulation we now have some insight bearing on the question raised in the first part of this paper namely Why is prog nosis so uncertain in coronary artery disease? One factor, perhaps the most important in determining the heart s capacity to develop collateral anastomotic circulation of functional significance is the anatomic pattern of the coronary bed This may be an heredi tary characteristic and if so it will explain the well known familial incidence of death from coronary dis ease Until we have a method of visualizing ade quately the coronary circulation during life, the fac tor of the anatomic pattern and the degree of coro nary arteriosclerosis existing in any given heart will remain as unknowns in *the equation and will con* tinue to make prognosis uncertain



Fig. 3. An example of left coronary arteriogram in which the left [illegible] supplies the left ventricle, the septum and part of the right ventricle. In addition, this [illegible] the effect of chronic [illegible] and the development of intercoronary anastomoses, particularly marked on the left ventricle. [illegible] coronary arteries [illegible] existence of [illegible]

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To all of these goes deep appreciation

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